A TEXTBOOK OF

SPECIAL PATHOLOGY

FOR THE USE OF

STUDENTS AND PRACTITIONERS

BY

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WITH 267 ILLUSTRATIONS IN THE TEXT AND 4 COLOURED
PLATES FROM ORIGINAL PREPARATIONS

SECOND EDITION

LONDON

WILLIAM HEINEMANN

(MEDICAL BOOKS) LIMITED

TO

THE MEMORY OF

WILLIAM SMITH GREENFIELD

M.D., F.R.C.P., L. AND E.,

FOR THIRTY-ONE YEARS PROFESSOR OF PATHOLOGY

IN THE UNIVERSITY OF EDINBURGH, OUR ,

TEACHER, "CHIEF," AND FRIEND,

WHO DIED AUGUST 12, 1919,

WE RESPECTFULLY AND

AFFECTIONATELY

DEDICATE THIS

BOOK

PREFACE TO SECOND EDITION

THE second edition of these volumes has been long overdue, and its appearance has been delayed by the many pre-occupations of the authors, including their service with the Royal Army Medical Corps during the War. In some ways, this has not been without benefit to the work, as they have been thus enabled to incorporate much of the new and valuable experience gained during and after the War by themselves and others.

The whole has been largely rewritten; and new matter of importance has been added, e. g. the chapter on Fever. As in the first edition, free use has been made of the published work of others, and, wherever possible, suitable acknowledgement of such sources has been made. We are specially indebted to Dr. John Milroy, of Queen's College, Belfast, for the thorough revision of the sections dealing with Chemistry, physiological and pathological : to Professor Ernest Glynn, of Liverpool University, for notes on the Pathology of the Suprarenal Glands : and to Dr. James Dawson, Royal College of Physicians' Laboratory, Edinburgh, for permission to use the beautiful illustrations of his Gold Medal Thesis on Inflammation. Mr. Richard Muir, of the Pathological Department, Edinburgh University, has again given us his invaluable help with the photo-micrographic and coloured illustrations; whilst the naked-eye photographs are almost entirely the work of one of the authors (W.E.C.D.). Many friends have helped us with proof-reading, and, in this connection, Professor Beattie wishes especially to thank Miss Thirza Redman, M.Sc. (Lond.), one of his assistants : and Dr. Carnegie Dickson gratefully acknowledges the help of Dr. J. Browning Alexander and Dr. F. W. Hamilton, and of his assistants, Miss M. Irene Wilson and Mr. Arthur Griffin.

Since the appearance of the first edition of this work, we have to record with deep regret the passing of him to whom it is dedicated, our old teacher, " chief," and friend, William Smith Greenfield, whose name will live as one of the great British Pathologists—perhaps, indeed, the father of modern British Pathology.

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J. M B.

W. E. C. D.

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August 1921.

PREFACE TO FIRST EDITION

IN the preface to our *Textbook of General Pathology* we stated that,
" if any excuse were necessary for adding another to the many textbooks
of Pathology, it would be found in the fact that the present volume is
based on the teaching of the Edinburgh school. This school, in which
the first chair of Pathology in the United Kingdom was founded, has
sent its teachers and students to all parts of the world, and thus of
necessity has had a considerable influence in moulding pathological
opinion. In spite of this, some fundamental points which have been
taught in Edinburgh for years, and which are founded on careful experi-
mental investigations, combined with a very extensive experience in
human morbid anatomy and morbid histology, have not, we think,
received sufficient attention. To mention only two points—on infarction
much is yet taught which is quite in opposition to experimental in-
vestigations, and the relation between certain diseases of the kidney and
arterial degeneration seems to be very imperfectly understood.

" The book is intended primarily as a textbook for medical students.
and practitioners, and we have, therefore, dealt fully with the more
important and fundamental points in Pathology, and have either omitted
altogether or dealt very briefly with rare and unimportant conditions.
Minute microscopic anatomy of abnormal structures and tissues has been
dealt with—though sometimes briefly, for we fully recognise that no
descriptive writing can be substituted for the actual specimen and the
microscope, and, moreover, the subject is fully dealt with in textbooks
on Morbid Anatomy and Histology." No attempt is made to deal with
such special subjects as Gynæcology and Diseases of the Eye and Ear;
and only brief reference is made to subjects which are fully treated of in
textbooks on Surgery and Surgical Pathology. Bacteriology is so well
dealt with in the many excellent textbooks now published, that, im-
portant as it is to, and inseparable though it be from, Pathology, we
have omitted it altogether as a separate subject.

We have especially to thank our old teacher and chief—Professor
Greenfield, of Edinburgh University—for placing the notes of his lectures
at our disposal. At his suggestion the work was undertaken, and without
his hearty co-operation and the benefits of his wide experience it would
have been impossible for us to overtake it. To acknowledge his help is
to us a pleasure, but it is, perhaps, even a greater pleasure to have the
opportunity of again bringing forward views founded on the results of

careful observation and experiment, which he has previously published and taught for many years, but which have not received the attention and recognition which they merit.

The compilation of a complete bibliography has not been attempted, though reference has been made to some of the more important papers consulted. We have made free use of the standard textbooks on pathology and medicine, and would specially acknowledge our indebtedness to the New Sydenham Society's *Atlas of Illustrations of Pathology, Fasciculus I, Diseases of the Kidney, A Résumé of the Present Knowledge of Renal Pathology,* by W. S. Greenfield, M.D.; and to various papers by H. J. Stiles, F.R.C.S.E., on the classification and spread of Mammary Cancer.

Almost all the illustrations are new, and are from specimens either specially prepared by or for us, or kindly lent for this work. The great majority of the photo-micrographs are the work of Mr. Richard Muir, Demonstrator of Pathological and Bacteriological Methods in the University of Edinburgh, and we desire to thank him for the care and trouble he has taken in their selection and preparation, the majority of the microscopical specimens being from his private collection. The · photographs of practically all the naked-eye specimens were taken personally by one of us (W.E.C.D.), and, where not otherwise acknowledged, are from specimens in his own private collection.

We have also to thank Professor Cunningham, Curator of the Edinburgh University Anatomical Museum, and the Fellows of the Royal College of Surgeons, Edinburgh, for permission to use specimens in their museum collections; and Mr. Henry Wade, F.R.S.C.Ed., Conservator of the Museum of the Royal College of Surgeons, Edinburgh, to whom we are indebted for the use of several specimens from his private collection, for purposes of illustration. To Sir Thomas R. Fraser, M.D., and Mr. H. J. Stiles, F.R.C.S.E., our thanks are due for permission to use photographs of certain of their cases: and also to Mr. Alexis Thomson and to Dr. R. A. Fleming, for the loan of microscopical preparations; to Drs. Lindsay Milne and Harvey Pirie, for their kind assistance in revising the sections on " Diseases of the Liver " and " Diseases of the Nervous System " respectively; to the editors and publishers of *Inter- . national Clinics,* for permission to utilise a paper upon the " Bone-Marrow," published by one of us in that periodical; and to Dr. A. Murray , Drennan and others, for their kind help in connection with proof-reading.

Lastly, it is a pleasure to acknowledge the uniform kindness and courtesy which we have received from our Publishers in connection with this work, and we thank them for the great care which they have bestowed upon its production.

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J. M. B.   ·

W. E. C. D.

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February 1909.

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SPECIAL PATHOLOGY

CHAPTER XIV

DISEASES OF THE CIRCULATORY SYSTEM

DEVELOPMENTAL ABNORMALITIES OF THE PERICARDIUM, HEART, AND GREAT VESSELS

MALFORMATIONS.—Complete absence of the pericardium is very rare, but an imperfect development of it is occasionally found. **Pouches** in and from it are described, but these are most commonly protrusions of the serous coat, either into the cavity, or outwards through a very thin or imperfectly developed fibrous coat.

Congenital defects in the heart itself, and in the great vessels, are far from uncommon; and, to understand these properly, some knowledge of the development of the heart and vessels is essential.

Development of the Heart and Vessels.—At an early period of fœtal life, the heart consists of a hollow tube, at first straight, and later S-shaped. Subsequently, the lower limb of the S becomes curved up behind, *i. e.* dorsal to, the upper limb, and grooves appear upon it externally, first a **transverse one** corresponding with the line of separation of auricle from ventricle, and then more or less **longitudinal ones** separating the auricles and ventricles of the two sides from one another. The cavities become divided by septa which develop from their lower and posterior walls. The **ventricular septum** is the first to appear. It, however, remains incomplete for a considerable time, a communication between the two ventricles persisting at its upper part. Later, this communicating orifice is closed. The auricular cavities become divided, in a similar way, by two partitions, which meet and partially overlap one another near the auriculo-ventricular septum. Union of these partitions is incomplete till after birth—the opening between them constituting the **foramen ovale.** The upper limb of the S forms the **truncus arteriosus,** and this also becomes longitudinally divided by a septum to form the **aorta** and the **pulmonary artery.** In the fœtus, the pulmonary artery and the descending aorta communicate with one another by the **ductus arteriosus,** which conveys, from the right ventricle, by way of the trunk of the pulmonary artery, into the descending aorta, most of the blood for distribution to the abdomen and lower limbs, as well as that distributed by the umbilical arteries.

Imperfect development, or **arrest**—complete or incomplete, as the case may be—**of the developmental process,** may take place at any stage, and this may be localised to one or more special regions or structures. Thus is to be explained the majority of the malformations of the heart and

great vessels, and, of these, only a very brief outline of the commoner varieties need be given.

Defects of the Ventricular Septum.—This septum may not be developed at all, or it may be incomplete. In the latter case, the opening between the two ventricles is situated usually at the upper part of the septum, where, even in the normal heart, no muscle-fibres exist, the dividing wall being composed of endocardium and a slight amount of intervening fibrous tissue alone—and hence the name **pars membranacea septi** or **undefended space** applied to this region. Sometimes, however, the opening is towards the posterior part of the septum. The body of the right ventricle may, in some of these cases, be atrophied, or almost entirely absent, and the foramen ovale is usually patent. In those cases in which the interventricular septum is completely absent, the body of the right ventricle is usually absent, but its infundibular cavity is well developed.

Defects in the Auricular Septum.—This septum may be entirely absent, or, in other cases, deficient only at its lower part. One of the commonest abnormalities is a patency of the **foramen ovale.** Frequently the aperture is small, very oblique, and practically so valvular in character that there is little or no communication between the blood in the two auricles. More rarely, the opening is directly patent, i. e. the septum ovale is itself absent in whole or in part, and there is thus a persistent communication, through which a mixing of the arterial and the venous blood takes place —a defect which is sometimes combined with congenital stenosis of the pulmonary valve.

Malformations in the Right Ventricle and Stenosis of the Pulmonary Artery.

1. **Subdivision of the Right Ventricle.**—This abnormality is compara- tively rare, and in it the ventricle is separated from its infundibulum by a **muscular partition**, the centre of which is perforated by a **foramen** varying in size. The **pulmonary cusps** may be normal, or they may be united, pro- ducing **stenosis** of the orifice. There may be an **interventricular foramen** just below the opening from the ventricle proper into the infundibulum. The **ductus arteriosus** and the **foramen ovale** may be patent. In an examination of such cases, Keith, to whose work we are greatly indebted for our information on these malformations in the heart, found that the fibrous margin of the **ostium infundibuli** was covered by vegetations.

2. **Congenital Pulmonary Stenosis.**

(a) Certain cases of this condition represent an arrest of development of the infundibulum; and the endocardium of the cavity is embryonic (fibro-cellular) in structure. The **ostium infundibuli** may be well marked, or represented by a mere thickening of the endocardium. The pul- monary valves are fused in the majority of cases, producing a greater or less degree of stenosis, and, in some, the interventricular foramen is present.

(b) In another group of cases, there has been an almost complete

developmental arrest of the infundibulum, and it may be represented by a mere slit or irregular chink situated at the orifice of the pulmonary artery and lined by thickened endothelium. The **orifice of the pulmonary artery** may .be very small, the fused semilunar valves just distinguishable, and the pulmonary artery represented by a mere fibrous thread at its origin. An **interventricular foramen** is always present, and, in some cases, the **ductus arteriosus** is also patent.

(c) **Stenosis** produced by mere **fusion of the semilunar valves** is generally attributed to fœtal endocarditis; but Keith points out that, though these stenosed valves are composed of dense laminated fibrous tissue at their margins, yet the body of the valves shews a reticulated tissue distinctly embryonic in character. Moreover, many of these cases shew a degree of arrested development of the infundibulum; and a developmental defect, rather than an inflammatory action, must be regarded as causal.

The effects produced by the narrowing of the pulmonary orifice depend, to a certain extent, on the period at which it takes place. If the stenosis occurs during an *early* period of development, the increased pressure in the right ventricle forces the interventricular septum to the left side, the aorta comes to open partly from the right ventricle, and the septum thus remains incomplete at its upper part. In the same way, the increased pressure in the right auricle interferes with the closure of the foramen ovale. Thus, in cases of congenital narrowing of the pulmonary artery, there are frequently associated with it an **incomplete ventricular septum** and a **patent foramen ovale.** If the stenosis takes· place *after* the interventricular septum is complete, increased work is thrown on the **right ventricle,** and it becomes **hypertrophied,** sometimes to a very marked degree. The **right auricle** becomes dilated, and the **foramen ovale** remains patent. If this patency is very marked, there usually result enormous **dilatation of both auricles,** especially of their appendices, and **hypertrophy of the left ventricle.** The **ductus arteriosus,** in such cases, frequently persists as an open channel.

Stenosis of the Aorta—a rare condition—is found at a point between the left subclavian artery and the opening of the ductus arteriosus, though it may also occur at the origin of the aorta. In the more usual form, the circulation is assisted by anastomosis between the subclavian artery and the thoracic and abdominal aorta, particularly by way of the internal •mammary and intercostal arteries. The stenosis. may be complete **(atresia).** A condition of **subaortic stenosis** has been described, in which, immediately below the orifice of the aorta, a fibrous collar surrounds the infundibulum of the left ventricle. This is formed by an irregular thickening of the endocardium, and, according to Keith, is due to a partial persistence of the *bulbus cordis,* which usually disappears on the left side of the heart.

ABNORMALITIES IN THE CUSPS OF THE VALVES.—The valvular cusps of the pulmonary and aortic orifices are sometimes abnormal in

number or in size.   There may be only two cusps—one generally being
larger than the other, and sometimes shewing evidence of partial
division.   Three cusps are occasionally present, but two may be large
and the third rudimentary; or there may be four, or even more, cusps.

Fenestration is very common, but usually unimportant, the lunulæ
being the parts generally affected.   Even when the cusps are normal
in number and in size, there may be **adhesions** between them, giving rise
to narrowing of the orifice.   These adhesions are generally regarded as
being due to endocarditis during intra-uterine life.   The curtains of the
auriculo-ventricular valves frequently become adherent to one another,
and produce narrowing of the mitral and tricuspid orifices.

**ABNORMALITIES IN THE LARGE VESSELS.—Doubling of the
aorta,** due to a persistence of the two developmental arches is
found; or the **right arch** may remain and form the aorta instead of the
left.   This is generally the case in **dextro-cardia,** but may occur inde-
pendently of that condition.   There may be **stenosis of the aorta** at, or
beyond, the junction of the ductus arteriosus; or the aorta may be nar-
rowed throughout its course.   This general narrowing or **hypoplasia** of
the vessel has been described as associated with, and even as causing,
chlorosis, but the aortic condition is probably congenital in origin.   Abnor-
malities in the origin and distribution of the larger arteries need not be
further referred to here, as such alterations do not, as a rule, give rise to
important disturbance of function.   In exceptional cases, the **left superior
vena cava** persists instead of the right, and the pressure of the heart
upon it may produce obstruction.   The **aorta** sometimes takes origin
from the infundibulum of the right ventricle, and the **pulmonary artery**
from the left ventricle.

MALPOSITIONS OF THE HEART are rare.   There may be complete
transposition—dextro- or **dexio-cardia—**but, in such cases, there is
generally, in addition, transposition of the other viscera.   The heart has
been found in the neck, in the middle line under the sternum, or imme-
diately under the skin; and, when in the latter position, the sternum
has usually a central longitudinal cleft.   The heart has been described
as lying below the diaphragm, between the stomach and abdominal wall,
and also in the neighbourhood of the kidneys, or even in an umbilical
hernia.

DISEASES AND INJURIES OF THE PERICARDIUM AND HEART

I. PERICARDIUM

Developmental abnormalities of this structure have been described on p. 497.

HYDRO-PERICARDIUM.—On *post-mortem* examination, a very small quantity of transuded fluid is usually found in the pericardial sac. This may be increased to a slight degree (a few ounces) before death, or there may be a great increase, producing a condition of **hydro-pericardium.** The nature of the fluid depends largely on the cause leading to its presence. The commonest examples of hydro-pericardium are seen in diseases of the kidneys, and in the " water-logging " of chronic heart-disease. In such conditions, the fluid is watery and of a light straw-colour, and usually contains little albumin. It may, however, be bile-stained, or it may contain blood derived from dilated vessels which have ruptured. More rarely, the fluid is milky in appearance and contains a large proportion of **chyle.** This is seen in cases where there is some pathological condition of the thoracic duct or of its tributaries.

In inflammatory conditions of the pericardium with effusion—to which the term hydro-pericardium is **not** applied—the fluid may be rich in albumin, and **blood** may be present in considerable quantities.

HÆMO-PERICARDIUM results from various causes :—

(*a*) **A punctured wound of the heart** usually gives rise to a considerable collection of blood in the pericardial sac, and, if the weapon or missile has passed through the pericardium, there may be also a considerable degree of hæmothorax. In the majority of cases of hæmothorax, however, it will be found that the hæmorrhage results from a wound of the lung, and that the blood does not come from the wound of the pericardium or heart. Wounds of the heart are usually fatal, but cases are recorded where recovery has taken place—even though the fluid in the pericardium has become infected with gas-producing organisms.

(*b*) **Rupture of the Heart.**—This generally, if not always, occurs in a heart which has been weakened by pre-existing disease. Degeneration and narrowing of the coronary arteries, with associated fatty degeneration and atrophy of the muscle-fibres, is the pathological condition usually found in such cases. Most commonly, the rupture is in the wall of the left ventricle, on its anterior aspect near the septum. It is very ragged in

appearance, and runs usually in the direction of the muscle-
fibres. The amount of blood in the pericardial sac varies from
a few ounces to a quart or more.

(c) **Rupture of an aneurism,** either on the intra-pericardial portion
of the aorta or on a coronary artery, will give rise to a similar
condition.

(d) **Petechial,** and sometimes **larger,** hæmorrhages are seen, especially
in the subepicardial tissues, **in toxic and bacterial diseases.**
In deaths from **asphyxia** (e. g. drowning), small hæmorrhages
may be seen (Tardieu's spots). These sub-epicardial hæmorrhages
occur mainly at the base of the ventricles and along the vessels.

(e) Other causes giving rise to an accumulation of blood, or of blood-
stained exudates, in the pericardium are mentioned under
hæmorrhagic pericarditis on p. 505.

" **MILK-SPOTS** " are irregular, whitish, thickened patches of fibrous
tissue, most commonly seen on the anterior surface of the right vent-
ricle, or on the anterior surface of the left ventricle near the apex.
They are less frequently found on the posterior aspect of the left ventricle
near the base of the heart. They may be merely opalescent thickenings
of the epicardium, or they may be distinctly fibrous and almost " carti-
laginous" in consistence. In many cases, they are the remains of a localised
pericarditis; but their situation, and their greater frequency in hearts
which are, or have been, hypertrophied or dilated, lend support to the
view that they may be caused by a constant and increased degree of
friction, giving rise to irritative overgrowth of the epicardium. These
milk-spots sometimes become œdematous in Bright's disease, etc. More
generalised thickenings of the epicardium are very common over dilated
auricles, dilated auricular appendices, etc., or along the lines of dilated
coronary arteries. The localised thickenings on the anterior surfaces of
the right and left ventricles were attributed to pressure and friction by
shoulder-straps worn by soldiers, and were in consequence known as
soldiers' spots.

INFLAMMATION :—

(a) **ACUTE PERICARDITIS** has always, for its cause, a bacterial or
a toxic irritant. It most commonly occurs during an attack of **rheum-
atic fever,** or such allied conditions as chorea, acute tonsillitis, etc., but
it is also common in **pneumonia,** especially in children, and occurs in
other **acute infective fevers,** in **septicæmia, pyæmia,** and, in general, in
any septic or bacterial disease. It also supervenes, though more rarely and
generally as a terminal event, in **Bright's disease,** in **gout,** in **diabetes,** in
scurvy, in **cancer,** and in **exophthalmic goître.** In all of these diseases,
there are organisms, toxins, or metabolic poisons of an unknown nature,
circulating throughout the system; and these organisms or poisons are,
directly or indirectly, the cause of the inflammation. **Acute pericarditis**

also arises by **local extension of inflammation** from a neighbouring area. Thus, inflammation of the **pleura,** of the **lungs,** or of the **mediastinal cellular tissue** or **glands** may involve the pericardium secondarily. Inflammation of the **myocardium** more rarely spreads to the pericardium, but **abscesses** in the heart-wall in cases of pyæmia, or abscesses in the mediastinum, or in the ribs, sternum, or elsewhere, may rupture into the pericardial sac and set up acute inflammation.

Fig. 232a.—Acute Pericarditis, shewing the irregular shaggy appearance of the recent inflammatory exudate.

Except for the fact that they are modified, in some degree, by the constant movements of the heart, the phenomena observed in acute pericarditis are practically identical with those seen in acute inflammation of any other serous surface, and are fully described in the chapter on **Inflammation** (see page 163 et seq.). The exudate into the sac may be very slight and may be converted into fibrin, so that there is no accumulation of fluid, and thus a condition of **dry** or **fibrinous pericarditis** results. This is seen especially in the inflammation occurring in Bright's disease, and sometimes in that following

pneumonia. More commonly, however, there is, in a greater or less degree, an effusion of fluid into the cavity. This effusion may be **serous, sero-purulent, purulent,** or **hæmorrhagic,** its character depending, to a certain extent, on the nature of the causal agent. Thus, in a pericarditis due to the rupture of an abscess into the sac, or when the condition is set up by the common bacteria of suppuration, the exudate is purulent or sero-purulent. In the most typical forms—**rheumatic** and **pneumococcal pericarditis**—the exudate is commonly sero-fibrinous in character, or slightly turbid. It is very rarely, if ever, purulent. Fibrin-formation tends to occur in a marked degree, especially in the pneumococcal cases, and both the peri- and epi-cardial serous layers become coated with whitish, shaggy masses of it, which, at first, are quite easily separated, but which, later, become vascularised and adherent. In its earlier stages, before such adhesions have taken place, this has been described as the " honeycomb " or " dog's tongue " condition, and is very aptly compared to the appearance presented by pressing together and then drawing apart two thickly buttered slices of bread (see fig. 232a).

In the early stages of the inflammation, the fibrin may form a very thin layer, and may be found only at the base of the heart, and around and between the great vessels. The causal organisms may or may not be present in the exudate. In the latter case, they are usually found **in** the tissues at or near the surface.

Terminations of Acute Pericarditis.—If the exudate is scanty in amount, or if the layer of fibrin is thin, **complete absorption** of the inflammatory products may take place, and the heart return to its normal condition—usually, however, with some evidence of slight chronic fibrous thickening, especially of the epicardium. **Adhesions,** however, are very apt to occur between the visceral and parietal layers of the pericardium, owing to the organisation of the exudate at an early period, the granulation-tissue thus formed becoming converted into dense fibrous tissue. These adhesions may extend over the surface of the whole heart, or may be limited in extent. They are more liable to occur in cases where there is little or no effused fluid to separate the inflamed surfaces, and at those parts of the heart which alter their relations to the parietal pericardium in least degree during cardiac movements, e. g. near the apex, over the left auricle, and at the base of the great vessels. Organisation of the fibrinous exudate may take place in localised areas over the epicardium, and thus may be formed the irregular, whitish areas of fibrous tissue, already described as one variety of **milk-spots** (p. 502). Sometimes, portions of the fibrin remain unabsorbed, and **calcification** occurs in these, as well as in the adhesions, and in the thickened patches on the surface of the heart or of the pericardium.

Associated Conditions.—Acute pericarditis may be associated with, and result from, the spread of inflammatory conditions in the adjacent tissues and organs; or, on the other hand, it is sometimes the primary

affection, and a secondary spread takes place from the pericardium to the pleura, lungs, or to the mediastinal tissues: A marked increase of the fibrous tissue in the mediastinum, with adhesion of the exterior of the pericardium to surrounding parts, is a common sequel, or these adhesions may be present without much fibrous mediastinitis. The invasion of the myocardium usually extends to a very slight depth; but, in rare cases, it penetrates throughout the muscle-substance, producing an extensive myocarditis, which may lead to serious derangements of the circulation, or to the death of the patient. The adhesions, to which reference has already been made, may be very dense, and constitute a serious impediment to the movements of the heart. Interference with the heart's action is also caused by the deposit of lime-salts in the fibrin-remnants, with the formation of a more or less complete calcareous investment or " case." These hindrances compel the heart to act under considerable difficulties, and **great hypertrophy and dilatation** (*cor bovinum*) are produced, especially if there are extensive adhesions to the chest-wall and lungs, as in cases associated with mediastinitis or inflammation of the mediastinal cellular tissue.

(*b*) **SUPPURATIVE PERICARDITIS (PYO-PERICARDIUM).**—This condition is generally the result of pyæmia or septicæmia, and is then due directly to septic infarction, or to the lodgment, in the pericardium or the superficial layers of the heart, of bacteria which produce suppuration. Abscesses are formed in the heart-wall, which spread to, or rupture into, the pericardial sac; or the surface of the pericardium is invaded by pyogenetic bacteria which bring about leucocyte-emigration and all the other phenomena of pus-formation. Suppurative pericarditis may also, however, be secondary to empyema, to pneumonia, or to abscess-formation in the lungs, mediastinal tissues, or bones, etc., of the thorax, to rupture of a gastric ulcer, and to other lesions. In its essential features, the suppurative form of pericarditis resembles the non-suppurative forms, but, as a general rule, it does not tend to spread to the heart-muscle.

Serous and **sero-fibrinous** exudates, in cases of acute pericarditis, may become purulent, but this is not common; and, in rheumatic pericarditis, suppuration, if it occurs at all, is very rare.

(*c*) **HÆMORRHAGIC PERICARDITIS.**—This form of pericarditis occurs specially in persons whose capillaries, on account of degenerative and other changes, easily rupture, and is most commonly seen in cases of scurvy, purpura hæmorrhagica, and hæmophilia. It is observed also in some chronic alcoholics, and in people who have been exposed to privation and cold. A similar condition sometimes supervenes in tuberculosis, sarcoma, or cancer of the pericardium or heart. The exudate may be almost pure blood, but all degrees of the condition, intermediate between this and a serum merely slightly blood-stained, may occur.

(*d*) **TUBERCULOUS PERICARDITIS,** though comparatively common

in cattle, is somewhat uncommon in man. It may be·secondary to tuberculous pleurisy or empyema, or to tuberculosis of the lung, mediastinal glands,' sternum, or ribs. Miliary tubercles, though they occur, are rarely found·in the pericardium in the course even of acute and wide-spread general tuberculosis. A very few scattered tubercles, usually along the coronary vessels, are not extremely rare in children. In exceptional cases, innumerable minute tubercles may occur. The pericardial surface is sometimes covered merely with a thin layer of fibrinous exudate, which, on naked-eye examination, is indistinguishable from the non-tuberculous variety. On the other hand, the exudate is not uncommonly thick and irregular, and numerous adhesions may exist between the two serous surfaces. The exudate may be **serous, purulent,** or **hæmorrhagic.** It is, in most cases, extremely difficult to demonstrate *B. tuberculosis* either in the fluid or in the fibrinous exudate. Usually, however, on microscopical examination, tubercle-granulations, with or without giant-cells, are found, either in the fibrinous exudate itself, or in the deeper layers of the pericardium.

Calcification is a common sequel of the tuberculous process, and the necrotic and destructive changes characteristic of tuberculosis cause very considerable damage to the heart.

(e) **PNEUMO-PERICARDIUM.**—This is uncommon and is due to the infection of the sac by one or more of the gas-producing organisms, e. g. *B. welchii (perfringens), B. œdematiens, Vibrion septique,* etc., introduced generally through a perforating wound.

In compound fracture of the ribs or sternum, penetrating wounds of the chest, etc., air may be introduced from without; and, in gangrenous or tuberculous cavities in the lung, in pyo-pneumothorax, in ulceration of the œsophagus, and in subdiaphragmatic abscess, communication may be established between the lung and the pericardial sac. In the majority of the cases, the effusion becomes purulent.

NOTE.—Pericarditis, in association with Polyserositis, has been referred to by several authors, and by some regarded as tuberculous. In our experience, if these cases are carefully examined, they will be found to be multiple foci of some bacterial infection—most frequently pneumococcal or streptococcal.

TUMOURS AND PARASITES.—Fibromas and **lipomas** may occur as **primary tumours,** but are extremely rare. **Secondary tumours** are also uncommon, but **lympho-sarcomas, melanotic sarcomas,** and **cancers** do occasionally occur. These arise by direct spread from surrounding parts, or they may be in the form of metastases from other organs. Secondary growths sometimes start in the heart-wall and invade the pericardium. **Epitheliomata** have been described as arising secondarily to epitheliomata of the lip, tongue, or œsophagus.

Hydatid cysts and **Cysticerci** are occasionally met with.

II. ENDOCARDIUM·

The endocardium consists of a delicate layer of flattened endothelial cells which lie on a very thin supporting structure of fibrous tissue. The valve-segments are prolongations of the endocardium, with, at places, a slight amount of fibrous tissue between the layers, and are non-vascular.

DEGENERATIONS :—

(a) **CLOUDY SWELLING** of the endothelial cells occurs in almost any infective disease.

(b) **FATTY DEGENERATION** may be associated with cloudy swelling, but also results from the action of cell-poisons such as chloroform or phosphorus. It is most commonly found near the base of the left ventricle and on the anterior flap of the mitral valve. The fatty areas are, usually, dull white or yellowish-white in colour, and lime-salts may be deposited in them.

(c) **CALCIFICATION** occurs sometimes as a sequel of fatty degeneration, or it · may follow other degenerative and chronic inflammatory changes. The cusps of the aortic valve and the anterior flap of the mitral are its most usual sites.

(d) **WAXY DEGENERATION** is said to occur in the sub-endothelial layer of fibrous tissue in the right auricle. If it occurs at all, it must be extremely rare.

(e) **GOUTY or URATIC** deposits are sometimes found in the mitral valve-segments or elsewhere. They are rare, and are generally associated with fibrous degeneration.

HÆMORRHAGES :—

Ecchymoses or **petechial hæmorrhages** are frequently found in the endocardium immediately under the endothelium, especially in the left ventricle. They are most commonly associated with similar hæmorrhages in other parts of the heart, particularly in the epicardium. They occur principally in septic diseases, and in such conditions as give rise to fatty or other degenerative changes in the endothelium of capillaries, as, for example, pernicious anæmia, phosphorus-poisoning, chloroform-poisoning, etc.

INFLAMMATION :—

Endocarditis may be acute or chronic. The acute form has been divided into two types—the " **simple** " and the " **malignant** " or **ulcerative.** Recent research has shewn conclusively that, in **both** forms, the valves are attacked by bacteria. **Vegetations** are formed, and these vegetations and the valves or other parts to which they are attached may, or may not, undergo softening, with the production of ulceration. Further, the organisms isolated from an ulcerative case have, experimentally, in one animal given rise to the ulcerative form of endocarditis, whilst, in another animal of the same species, a simple endocarditis has

resulted.   Thus, it will be seen that the distinction usually made between the two forms, though very convenient clinically, has no pathological basis, and, moreover, all intermediate degrees between the two extremes occur.   At the same time, it is convenient, for purposes of description, to describe the two forms separately.

(a) **SIMPLE (NON-ULCERATIVE) ACUTE ENDOCARDITIS.**—This form occurs most commonly in **acute rheumatism,** and in allied conditions such as **chorea.**   About 80 to 90 per cent. of the cases are rheumatic in origin.   Cases have been described as following **scarlet fever** and some other infectious diseases, and also as occurring during, and apparently associated with, **Bright's disease.**   In definitely rheumatic cases, several observers have described the presence of bacteria, and the organism which has received the greatest support as the cause of the disease is a small diplococcus described by Wassermann, and afterwards by Poynton and Paine and others.   This diplococcus has been isolated in cases of acute rheumatism; and, following upon its inoculation into rabbits and monkeys, typical **rheumatic arthritis,** accompanied, in many cases, by endocarditis, has resulted.   Much evidence has been brought forward in support of the causal relationship of this organism to rheumatism, but at present the case remains *sub judice.*   The experimental work done by one of the writers [1] leads us to support very strongly the view that the *Diplococcus* or *Streptococcus rheumaticus* is a causal factor. This organism may be, and probably is, a common inhabitant of the mouth and the intestine.   Under certain circumstances, it assumes a more or less virulent character.   This increased virulence may be inherent in the organism itself, or it may be a result of the lowering of the vitality and resisting power of the individual attacked.   According to this view, the endocarditis of scarlet fever or of any infectious disease, or even that seen in Bright's disease, may have as its primary cause the same organism, which, under different circumstances, can give rise to acute rheumatism and chorea, and even to ulcerative endocarditis and septicæmia or pyæmia.   There is also evidence that acute endocarditis of a non-ulcerative type is set up by the *Pneumococcus,* the *Gonococcus,* and other common pathogenetic bacteria; but such cases are comparatively rare, and the commoner result of infection by these organisms is an ulcerative and destructive change in the valves.   The minute vegetations which are sometimes seen on the valves in debilitating diseases, such as cancer, pulmonary tuberculosis, diabetes, etc., may also be bacterial in origin, the low bactericidal power of the blood in these cases predisposing to infective conditions.

Morbid Anatomy and Histology.—The valves are the special sites of endocarditis, though, in some cases, there is a spread to the adjacent parts of the endocardium.   During **extra-uterine** life, the valves of the

[1] Beattie, *Jour. Path. and Bact.,* March 1904; *Jour. Med. Research,* January 1906; *Jour. Exp. Med.,* March 1907.

left side of the heart are more frequently affected than those of the right side, and the mitral more commonly than the aortic, though both may be attacked at the same time. After birth, it is rare to get a primary endocarditis affecting either the tricuspid or pulmonary valves alone; but, in intra-uterine life, the valves on the right side seem specially to suffer. This variation in incidence, occurring in these two periods, is probably to be explained by the fact that the strain is greatest on the right side during intra-uterine, and on the left side during extra-uterine, life, this strain rendering the valves more vulnerable to attack by bacteria. The affected valves — which often shew a slight pinkish tint from blood-staining — become **swollen** and **translucent**, especially at or near their free margins, which usually present an irregular, beaded appearance. If, as may occur especially along the margins of contact, the swollen and softened endothelial cells become loosened and detached —or even without the loss of the covering endothelium—the blood-platelets tend to adhere to the roughened and damaged surface, agglutinating into small

FIG. 233.—Acute Endocarditis, with vegetations on the anterior cusp of the mitral valve and on the aortic valves. (Edinburgh University Anatomical Museum. Catalogue No., Cir. F. b. 4.)

masses, at first, papillary in character and resembling a delicate velvet-pile; but later, becoming increased in size by a further deposit of platelets. Leucocytes become entangled among these, and may break down and bring about the formation of fibrin. Thus, the vegetations enlarge and become more opaque, and of a whitish or yellowish-white colour, in some cases attaining a considerable size. **Microscopically,** they are seen to be non-vascular, homogeneous masses composed of fused blood-platelets and fibrin. Bacteria are usually present at some stage in the process of formation,

but they may be destroyed or so altered that they are not seen after death. On the mitral segments, the vegetations are almost invariably on the auricular surface near the free margins; and, on the aortic cusps, they are most commonly found on the ventricular aspect, at or near the edges of apposition, along the lunulæ and on the corpora Arantii. If the inflammation is intense in the mitral segments, it may spread to the **chordæ tendineæ,** and even to the **papillary muscles** and neighbouring endocardium. These structures become swollen• and infiltrated with inflammatory products, and the chordæ tendineæ sometimes rupture. From the aortic cusps, there may be a spread to the wall of the ventricle, but this occurs chiefly in the ulcerative type.

Fig. 234.—Acute Ulcerative Endocarditis of Aortic Valve, with extensive destruction and perforation of the cusps. (Edinburgh University Anatomical Museum Catalogue No., Cir. F. b. 1.)

(b) **ULCERATIVE, "MALIGNANT" or "SEPTIC" ENDOCARDITIS** may be divided into two forms, a **primary** one resulting from the direct action of bacteria in pyæmia, septicæmia, etc., and a **secondary** form where, in the course of, or as a sequel to, an acute, simple endocarditis, ulceration supervenes. The changes produced in the two forms are practically identical in character, and the same organism may cause either. It is therefore, unnecessary, to maintain the distinction. Of the organisms found in the ulcerative variety, probably one of the most important is *Pneumococcus,* but *Staphylococcus pyogenes aureus, Streptococcus pyogenes, B. coli, B. typhosus, Gonococcus, Streptococcus rheumaticus,* and other organisms may be causal. Some of these, especially *Gonococcus* and *Pneumococcus,* also give rise to arthritis, and this may be associated with the endocarditis.

It has been shewn by experiment that *Streptococcus rheumaticus,* isolated from a case of simple rheumatic endocarditis in the human subject, may give rise to either a simple or to an ulcerative endocarditis in different animals of the same species; and it is also an established fact that an originally simple endocarditis may assume, later, the ulcerative or "malignant" type.

Morbid Anatomy and Histology.—The valves on the left side of the heart are most commonly attacked in both types of the disease, but an affection of the valves of the right side more frequently arises in the ulcerative than in the simple type.

The inflammation in the ulcerative variety of the disease is usually much more intense and more widely spread, and the vegetations are commonly **larger,** much **softer,** and more **friable** than in the simple form. They frequently extend to the endocardium of the adjacent heart-wall

—especially to any part coming in contact with the valves or vegetations upon them—and to the aorta. **Ulcerative** and other **destructive** changes are common both in the valves and in the heart-wall, leading to **perforation** of the valves, and, in very severe cases, to perforation of the wall of the ventricle at the *pars membranacea septi*, or of the aorta into the pulmonary artery at the origin of the former vessel. **Aneurisms** of the **valves** may be produced, and these, at a later period, may rupture, causing perforation. Such aneurisms are found especially on the mitral and aortic segments. In the case of the mitral, they usually occur on the
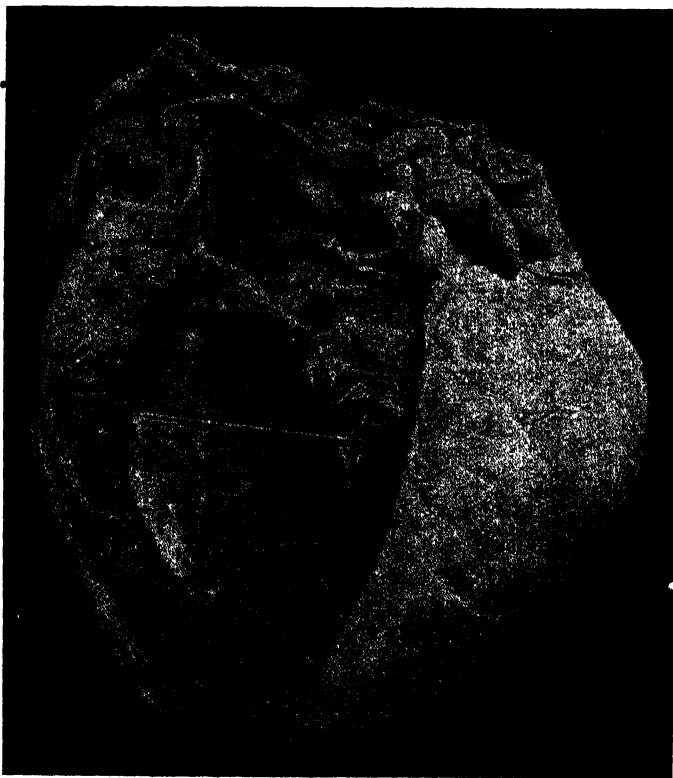
Fig. 235.—(1) Rupture of a previously diseased aortic cusp. (2) Thickened cusp still in position. (3) Anterior cusp of mitral valve. Note the marked dilatation of the left ventricle. (Specimen lent by the late Professor Greenfield.) *

anterior flap, are directed upwards towards the auricle, and may perforate into it. On the aortic segments, they are generally directed downwards, and perforate towards the ventricle. When such perforation has occurred, a ring of vegetations is usually found projecting from the surface around the orifice. Aneurisms are also formed in the wall of the aorta, near its origin, or in the wall of the heart close to the origin of the aorta, and these project towards the pulmonary artery or the right ventricle, into which they may open—though rupture into

the pericardium is more usual. In some cases, rupture of the valves, or of the chordæ tendineæ, occurs; and, especially in those which are secondary to old endocarditis, the inflammation may spread for a considerable distance into the ventricular wall, and give rise to an extensive myocarditis. On account of the destructive changes which take place in the valves, the softened and friable vegetations, or fragments of these, are very easily detached, and may give rise to multiple emboli in the vessels of the spleen, kidney, brain, intestine, heart, etc., and, in these organs, produce such conditions as septic infarcts, abscesses, ulceration, or gangrene.

Sequelæ of the inflammatory process.—If slight, the inflammation generally subsides and the parts return to their normal condition. More usually, however, there is some permanent damage to the valves, and this is generally increased by **recurrent** attacks, which, especially in rheumatic endocarditis, are very common. Among the more usual resulting changes are :—

i. **Adhesions,** which tend to form first at those parts of the valve where the segments are nearest to one another. The **mitral valve-segments** become adherent at the free lateral margins, between the adjacent chordæ tendineæ, and thus give rise to a **funnel-shaped narrowing** of the mitral orifice. At a later period, marked **shrinking** and **fibrosis** take place in the segments, the chordæ tendineæ become bunched together, thickened, shortened, and, it may be, adherent at places, producing a small opening at the lower end of the funnel (*see* fig. 237). On the other hand, the segments may become partially united on their adjacent surfaces in such a way that a slit-like or crescentic opening is formed —the so-called **button-hole form of mitral stenosis** (*see* fig. 240). One or other of these types of mitral stenosis is a common result of endocarditis, whereas incompetence of the valve, unassociated with stenosis, is a somewhat rare sequel. In the **aortic valve,** the adjacent cusps may become adherent to one another, producing stenosis of the orifice.

ii. **Contraction and thickening of the valves** are common results of an acute endocarditis, for, during the inflammatory process, there is produced in the valve a form of granulation-tissue, which becomes organised and transformed into fibrous tissue. The thickening and contraction, thus produced, gives rise to deformity of the valve-segments and consequent incompetence of the valves. This **incompetence** is more particularly liable to occur in the aortic valve. In the case of the auriculo-ventricular valves, the fibrosis and contraction spread usually to the chordæ tendineæ and to the papillary muscles.

iii. **Calcification.**—After the inflammatory process has subsided, secondary degenerative changes are very liable to occur, and lime-salts are deposited in the degenerated areas. This calcification causes rigidity, roughness, and irregularity of the valves; produces incompetence

and stenosis; and, on account of the damage to the endothelium, leads to the formation of thrombi (vegetations) on the segments.

SUBACUTE BACTERIAL ENDOCARDITIS.—Several authors have described, under this name, a form of endocarditis, which may be said to occupy a position midway between the simple and the malignant or ulcerative type. The onset is insidious, the condition frequently arising in patients already suffering from cardiac disease itself—pre-existing valvular lesions, hitherto typically quiescent, becoming the seat of a fresh infection. The valves involved are the aortic and the mitral, the former more frequently than the latter. The vegetations, which are usually extensive, vary in appearance and consistence, and tend to spread from the primary seat of infection to the adjacent endocardial wall and to the neighbouring valve. In old cases, the vegetations become firm, and often calcareous; but, in the early stages, they are extremely friable. In most instances, the heart is enlarged. Detachment of vegetations, with consequent **embolic infarction** in various organs, e. g. brain, spleen and kidney, is common. Libman claims that 95 per cent. of such cases are due to a hæmolytic *streptococcus*, and the remaining 5 per cent. to other bacteria, e. g. *B. influenza, gonococcus, pneumococci*, etc. It is generally recognised that, in all inflammatory conditions, subacute cases occur, and that, especially in the heart, subsequent attacks are very

Fig. 236.—Chronic Endocarditis of the Aortic Valve, with nodular thickening and calcification, and shewing adhesions between the cusps. (Edinburgh University Anatomical Museum. Catalogue No., Cir. F. o. 3.)

liable to take place on valves already damaged by a previous attack. From the pathological standpoint, therefore, there seems very little justification for the term "subacute" being applied to such cases, though, from the clinical side, the term may be useful. It should, however, be clearly understood that this disease is not a newly recognised one, and that all the *post-mortem* appearances have been described under acute endocarditis and its sequelæ.

CHRONIC ENDOCARDITIS.—In this condition, the affected parts of the valves are thickened and opaque; and sometimes, along the edges, firm, nodular elevations are found. **On microscopical examination,** the valves are seen to be the seat of fibrous-tissue formation in which degenerative changes occur, and which, by its contraction, produces shrinking, and perhaps puckering, of the valves, and impairment of their function. In the degenerated areas, in the early stages, the sub-endothelial cells may shew necrosis and fatty degeneration, while, at a later stage, lime-salts are deposited, and the valve-segments become much thickened, very rigid, and even almost entirely calcified. The chordæ tendineæ, which often share in the process, become shortened and thickened. As a

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result of these changes, stenosis of the orifices and incompetence of the valves may be produced.

The **aortic cusps** are most frequently affected, and the condition is specially seen along their margins of contact—at or near the corpora Arantii—and along the attached borders. In the **mitral valve,** the changes are usually not so marked and are often limited to the anterior curtain, especially towards its base near the aortic valve, at which part it is exposed to the strain, not only of the auriculo-ventricular, but also of the ventriculo-arterial, blood-stream.

FIG. 237.—Chronic Endocarditis of the Mitral Valve, with shortening and adhesion of the chordæ tendineæ, and extreme stenosis of the orifice. There are small recent vegetations on the aortic cusps. (Edinburgh University Anatomical Museum. Catalogue No., Cir. F. f. 2.)

Chronic endocarditis may be a **sequel** of acute endocarditis, or it may be a **primary** degenerative condition, produced gradually by the action of some irritant present in the circulating blood. Thus, it occurs in gout, in Bright's disease, in chronic alcoholism, chronic lead-poisoning, and syphilis. In old age, it occurs as a senile degenerative condition—**Chronic-Fibroid Degeneration**—and is frequently associated with similar degenerative conditions in the vessels.

TUBERCULOSIS.—Tubercles, usually of small size and few in number, occasionally occur in the endocardium, especially on the ventricular septum. Rarely, a more extensive tuberculous endocarditis is found.

VALVULAR DISEASE OF THE HEART

Having studied endocarditis and its effects upon the various valves of the heart, it is convenient at this point to consider the **causes** of the condition, and the **effects** produced on the heart itself, and also on the circulation, by those lesions which give rise to **obstruction** of an orifice, to **regurgitation** through the orifice, or to a **combination of both** of these conditions.

Fig. 238.—Great Hypertrophy (combined with Dilatation) of Right Ventricle in Mitral Stenosis. Note the comparatively small size of the left ventricle.

1. THE MITRAL VALVE

(a) **MITRAL STENOSIS.**—This is most commonly the result of an attack, or series of attacks, of **endocarditis,** leading to adhesion of the valve-curtains to one another, and to narrowing of the orifice.

If the stenosis is **extreme,** and if there is **no** regurgitation, the **left ventricle** may become **atrophied,** owing to the fact that very little blood passes into it, and that, in consequence, its work is very much lessened, this diminution in functional activity leading to atrophy. The blood-pressure in the **left auricle** is raised, and the auricle, having to drive on its blood against a greater resistance, becomes **dilated** and **hypertrophied.** It becomes lengthened in its vertical diameter, and assumes a some-what conical shape; and its appendix is enlarged and elongated, and may extend round in front of the pulmonary artery, or even be

doubled on itself like a horseshoe. **Thrombosis** may occur in' the appendix or in some other part of the auricle; and the endocardium of the chamber becomes **thickened** and shews an opaque-white, fibrous appearance. Further, the increased resistance in the left auricle leads to venous congestion in the lungs, and the extra pressure thus produced in the pulmonary vessels comes to bear upon the right side of the heart. The **pulmonary arteries** become **dilated and thickened**, and may shew a considerable degree of atheroma. The **right ventricle** undergoes **dilatation** and **hypertrophy**, assuming a somewhat quadrilateral shape, due in part to dilatation and thickening of the conus. The **tricuspid** valve, on account of the dilatation of the ventricle and the inability of its segments to close the orifice, may become **incompetent. The right auricle**, as a result, undergoes **dilatation** and **hypertrophy**; its endocardium becomes **thickened**, as does that of the right ventricle, and thrombosis may occur in the auricle, especially in its appendix, which is also dilated and elongated. Obstruction to the systemic venous return into the right auricle is thus brought about, and the condition of **chronic venous congestion**
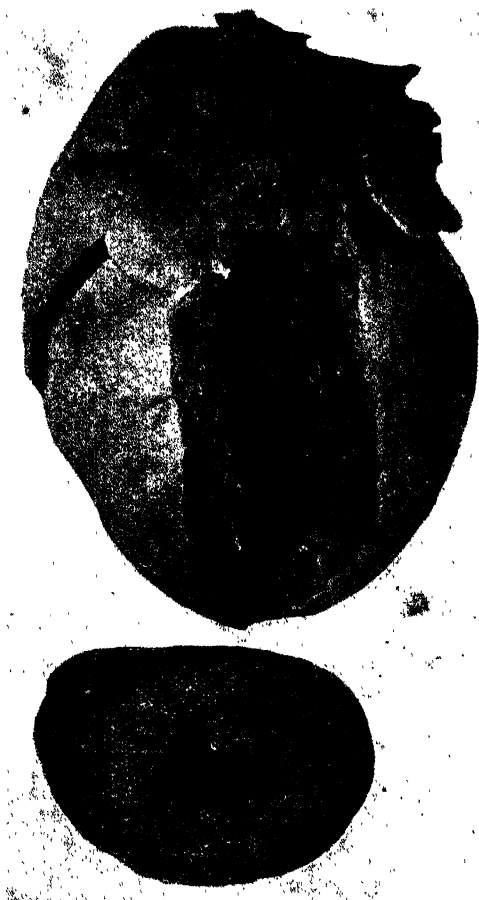
Fig. 239.—Hypertrophy and Dilatation of Left Ventricle in Aortic Disease. Below is a transverse section (near the apex of the ventricles) of a similar specimen.

occurs in the various organs and tissues.

(b) **MITRAL INCOMPETENCE** is usually due to old endocarditis with a combination of **retraction** and **contraction** of the valve-segments, though it also is a sequel of dilatation of the left ventricle and the valve-ring. As a consequence of the condition, the **left auricle** becomes **dilated**. There may be some **hypertrophy**, but this is not a special feature of the incompetence. The **left ventricle** undergoes **dilatation**

and **hypertrophy.** The remaining chambers of the heart, as well as the lungs and other viscera, show changes almost identical with those seen in mitral stenosis.

In cases of mitral stenosis or mitral incompetence in which a general condition of chronic venous congestion is produced, the heart-muscle, especially of the right ventricle, feels very tough and indurated— a condition which is sometimes mistaken for interstitial myocarditis. The firmness is really due to an over-filling and distension of the blood-vessels, and a very similar physical condition may be produced experimentally by injecting the coronary arteries with water. The condition is that of chronic venous congestion of the heart-muscle.

2. THE AORTIC VALVE

(a) **AORTIC STENOSIS.**--This is generally a sequel of endocarditis. On account of the narrowing of the orifice, the left ventricle requires to exert greater force in order to expel its blood. The result is a gradual elongation and slowly-produced thickening of the muscular wall of the **left ventricle.** There may be little or no **dilatation,** so long as the hypertrophy is sufficient to "**compensate**" for the increased resistance; but, if compensation fails, **dilatation** of the left ventricle also ensues, and, eventually, there arise conditions similar to those seen in cases of mitral incompetence.

(b) **AORTIC INCOMPETENCE.**--This may be produced by endocarditis (pp. 510 *et seq.*), by degenerative changes in the valves, or by rupture—usually the result of a violent strain, a crushing injury to the body, or a blow—of valves, especially those which are weakened by degenerative changes or by simple endocarditis (*see* figs. 235, 236, 237). It is much commoner than stenosis, though the two conditions may be, and frequently are, associated. As a result of the incompetence, the **left ventricle** becomes **hypertrophied,** and, if the regurgitation of blood is considerable, the degree of **dilatation** may also be very great. The dilatation, by stretching of the auriculo-ventricular ring, leads to secondary incompetence of the mitral valve, with all its resulting effects on the heart and other organs. Further, on account of the regurgitation of blood, in incompetence of the aortic valves, the coronary arteries do not get properly filled, and, as a result, the nutrition of the heart-wall suffers. The muscular substance is not now able to respond to the extra strain thrown upon it, and still further dilatation of the various chambers follows.

3. TRICUSPID VALVE

(a) **TRICUSPID STENOSIS** may result from ulcerative endocarditis at any time of life, but is most commonly caused by simple endocarditis, either during intra-uterine or very early in extra-uterine life. According to Greenfield—and our own observations confirm his teaching—it is almost constantly associated with mitral stenosis, and, further, the

tricuspid orifice is never so much contracted as the mitral. The results of this double stenosis are a **vertical elongation** of both auricles, **dilatation** of their cavities, **hypertrophy** of their walls, and an **elongation** of their appendices, which may almost meet on the anterior aspect of the heart. Usually, the ventricles are not much affected, though there is sometimes a slight amount of dilatation. The double stenosis, unless extreme, produces comparatively little effect on the general and pulmonary circulations, the stenosis of the tricuspid orifice seeming to protect the lungs from the effects of the mitral lesion, and helping to balance the blood-flow on the two sides. This condition is found in a proportion of cases of exophthalmic goître (Greenfield).

(*b*) **TRICUSPID INCOMPETENCE** may be produced by ulcerative
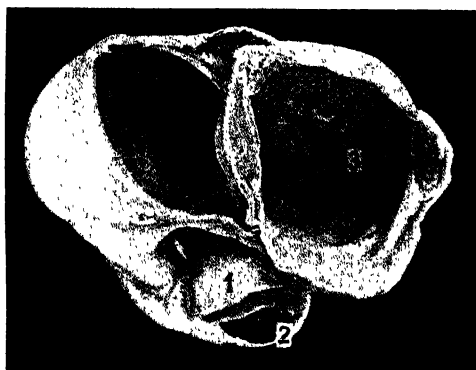
Fig. 240.—Mitral and Tricuspid Stenosis from a case of Exophthalmic Goitre.
1. Aorta.　2. Pulmonary artery.　3. Mitral orifice.　4. Tricuspid orifice.

endocarditis; but by far the commonest cause is dilatation of the **right ventricle,** and, consequently, of the valve-ring, to such an extent that the valve-segments are unable to close the enlarged orifice—complete closure being also prevented by the chordæ tendineæ, which are now of insufficient length. This incompetence may be, as has been pointed out, a result of the dilatation following mitral disease, but dilatation from any cause, *e. g.* that following obstruction in the lungs by local pulmonary disease, may produce it.

4. PULMONARY VALVE

(*a*) **PULMONARY STENOSIS.**—This may, during **extra-uterine** life, be a result of ulcerative endocarditis. Generally, however, the condition is produced during **intra-uterine** life, and is caused by an attack of fœtal endocarditis, or may be the result of mal-development. If it occurs before the inter-ventricular septum has been completely formed, the further growth of the septum may be arrested, and a permanent communication will be established between the two ventricles. If it occurs at a later period, the chief effect is an enormous **hypertrophy of** the **right**

ventricle. In such instances, the **foramen ovale** is frequently found to be **patent.** In some extreme cases, there is very marked deviation of the septum between the aorta and the pulmonary artery, and the aorta opens from both ventricles.

(*b*) **PULMONARY INCOMPETENCE,** from disease or from tearing of the cusps by severe crushing injuries to the chest, may occur, but is very rare, and does not call for further description.

THROMBI IN THE HEART

These may be divided into three main classes :—

(1) Irregular nodular or papilliform thrombi or **vegetations,** which form on the valves, have been described under **Endocarditis.**

(2) **Globular thrombi** are rounded or oval bodies which are generally soft or even fluid in the centre. They vary in size, and may be so large as almost to fill a cavity of the heart. They are found mainly in dilated and hypertrophied chambers, where the blood-flow is more or less interfered with, or where eddies are formed. Thus, they are found at the apices of the ventricles, or entangled in the columnæ carneæ, and in the auricles where there is obstruction to the outflow of blood from narrowing of the valvular orifices.

(3) **Ante-mortem thrombi** and **post-mortem clotting** are fully discussed under **Thrombosis** (*see* p. 141).

III. MYOCARDIUM

ATROPHY.—In old age, the heart may be comparatively healthy and vigorous, atrophy not being so common in it as in some other organs of the body. When it does occur in old age, the probable explanation is that the heart, on account of the degenerative changes in the vessels throughout the body, has to work against greater resistance, and, therefore, first undergoes hypertrophy : and that this condition of hypertrophy will be maintained until it has reached a certain limit, after which the heart-muscle becomes exhausted, atrophy then supervening. The period at which this exhaustion takes place varies, and is dependent, to a considerable extent, on the nutritive capacity and blood-supply of the heart-muscle. If the coronary arteries are degenerated, and the vascular supply of the heart is thus impaired, atrophy is liable to occur at an earlier stage. The wasting usually affects all the structures of the heart, the surface becomes wrinkled, and the arteries tortuous. The muscle assumes a dark-brownish colour—**Pigmentary Degeneration**—and the whole heart is atrophied, hence the name **Brown Atrophy** applied to this condition (see p. 72).

On **microscopical examination,** the muscle-fibres are lessened in diameter, and an excessive amount of yellowish granular pigment may be seen in the protoplasm around, and especially towards the poles, of their nuclei (*see* Plate III, fig. 4, p. 74.).

The atrophy may be extreme, the heart being reduced, even to one-third of its normal weight. This condition is often well exemplified in the atrophy seen in wasting diseases, e. g. cancer, diabetes mellitus, etc. In chronic pulmonary tuberculosis, the same condition is sometimes seen, but, in this disease, hypertrophy and dilatation, associated with the vascular obstruction in the lungs, are frequently pronounced pathological changes.

The atrophy may be **localised,** as a result of loss of functional activity in any part of the heart. Thus, in extreme mitral stenosis, the left

Fig 241.—Fatty Degeneration of Heart-Muscle, from a case of pernicious anæmia. Stained with osmic acid. × 400.

ventricle receives a greatly reduced volume of blood through the narrowed orifice, and, in consequence, has its work much diminished, and may undergo very considerable atrophy. Or again, especially in the right, but sometimes also in the left, ventricle, where hypertrophy has lasted some time, a supervening atrophy of the papillary muscles and the columnæ carneæ is a very constant feature.

DEGENERATIONS :—

(a) **CLOUDY SWELLING** of the heart-muscle is comparatively common in **acute infective diseases,** especially diphtheria, scarlet fever, septicæmia, pneumonia, etc. It occurs most markedly in the muscle-

fibres of the left ventricle. **To the naked eye,** the myocardium usually shews a cloudy pinkish-red opacity and loss of the reddish-brown, semi-translucent appearance characteristic of the *normal heart-muscle. In* many cases, however, there are little or *no obvious naked-eye charac-* teristics, but, **microscopically,** the muscle-fibres are swollen and are closely packed together. The striation may be more or less obscured, the nuclei may shew karyorrhexis, and coarse granules are sometimes seen scattered in the cell. In the connective tissue of the narrowed inter-muscular spaces, there may be a few leucocytes. In severe, advanced

Fig 242.—Fatty Degeneration of Heart-Muscle Stained with osmic acid. × 200.

cases, the muscle-fibres are semi-translucent and swollen, and may even shew transverse fracture or fragmentation —an appearance very similar , to **Zenker's degeneration.** Cloudy swelling of the heart-muscle is very frequently combined with some degree of acute fatty change.

(*b*) **FATTY DEGENERATION** of the heart is extremely common, especially in minor degrees, and is found as a result of any debilitating disease, and also as a senile change. In a more pronounced degree, it occurs in diseases such as **pernicious,** and other forms of, **anæmia, leukæmia,** and some **acute fevers,** where there is a marked deterioration of the blood, and where some toxin is circulating in the system. The toxin or other poison is probably the principal causal factor. The change is seen in an

extreme degree in **phosphorus-** and **chloroform-poisoning,** and is also a pronounced feature of **chronic alcoholic poisoning.** The presence of the condition is indicated by a varying degree of a diffuse yellowish colour throughout the muscle-fibres (**diffuse fatty degeneration**), often more marked in certain areas than in others, or by pale or yellowish-white irregular patches in the fibres which lie immediately under the endocardium, especially those of the papillary muscles and the wall of the left ventricle, particularly the septum. This patchy distribution or mottling is very well seen in the heart in some cases of pernicious anæmia, and has been described as the " **thrush-breast** " appearance. The degenerated muscle is

Fig. 243.—Fatty Infiltration of Myocardium of Right Ventricle. The muscular fibres have been almost completely replaced by fat.

usually flabby and friable and feels greasy to the touch. On **micro-scopical examination,** the fat-globules are seen, very often in rows in the muscle-fibres, replacing some of the fibrils (*see* figs. 241 and 242). Fatty degeneration may predispose to rupture of the heart-muscle.

(*c*) **ADIPOSITY,** or, as it is very generally called, **FATTY-INFILTRA-TION,** of the heart, is an abnormal increase of fat in situations in which it is normally present, and an infiltration of this fat into the connective tissue lying between the muscle-bundles. As a result, atrophy of the muscle takes place, and at first the superficial, and then the deeper, layers of the muscular wall are largely replaced by adipose tissue—the condition occurring progressively from without inwards. In extreme cases, the fat appears in patches immediately beneath the endocardium. It is usually best seen in the right ventricle, especially towards its apex, and also in the anterior wall near the interventricular septum, along the line

of the coronary artery in that position. It is also often well marked in the ventricular wall just below the auriculo-ventricular groove (see fig. 243). All stages of the condition may be traced—from the hearts in which the sub-epicardial fat is increased but shews no infiltration, through those in which the line of demarcation between fat and muscle has become lost, up to those in which the entire muscular wall is, in certain areas, replaced by adipose tissue. This adiposity of the heart may be merely part of a general obesity, but, in other cases, it occurs without any increase of adipose tissue elsewhere. Thus, it may be seen in old and debilitated persons, or in those suffering from some emaciating disease such as phthisis or cancer. In such cases, it is probably a sequel, rather than a cause, of the wasting of the muscle, and appears to be a process parallel with what occurs in voluntary muscle which has lost its function. One of the commonest causes of fatty infiltration of the heart is degeneration, thickening, and narrowing of the coronary arteries (see below). It is common in alcoholics, and is then often associated with atheroma.

(d) **WAXY, and HYALINE and CALCAREOUS DEGENERATIONS** are said to occur, but are very uncommon.

VASCULAR DERANGEMENTS :—

(a) **CHRONIC VENOUS CONGESTION** of the myocardium is a common change, and is especially associated with valvular disease and with chronic venous congestion in other organs. The muscle, especially that of the right ventricle, becomes extremely firm and indurated, and, to the naked eye, the wall of the ventricle appears hypertrophied. **On microscopical examination,** however, the induration and increase in thickness are found to be due to a distension of the minute veins and capillaries, and not to hypertrophy of the muscle-fibres or to increase in the amount of the inter-muscular fibrous tissue.

(b) **STENOSIS AND OCCLUSION OF THE CORONARY ARTERIES.** Though minute anastomosing channels exist between branches of the coronary arteries, this anastomosis is so scanty and imperfect that these vessels must be regarded as among the **end-arteries** of Cohnheim. They are peculiarly liable to degenerative changes, and are among the commonest sites of **atheroma.** The atheromatous changes may occur throughout the course of the artery, or they may be confined to the opening from the aorta or to the first half inch of the vessel. The results of these degenerative changes are, **narrowing, or even complete obstruction,** of the vessel or of some of its branches, and serious **interference with the nutrition of the heart-muscle.** , The muscle-cells show evidence of fatty degeneration and atrophy, and, eventually, the cells are replaced by fibrous tissue. These changes are usually patchy in distribution. **Fatty infiltration is** also a common sequel of such arterial disease. Further, **thrombosis** may occur in the degenerated vessels, producing **complete obstruction.** Block-ing of the coronary arteries may also be caused by portions of clot or

thrombi or vegetations which have become detached from their site of origin and carried as emboli into the arteries. If these emboli are septic, **abscesses** may be formed in the heart-muscle.

The Effects of Obstruction will vary somewhat according to the suddenness of the onset and the size of the obstructed vessel. Sudden obstruction of an important branch, however caused, will, if not immediately fatal, give rise to **infarction** in the heart-wall. The vessel most usually affected is the descending branch of the left coronary artery, and, consequently, the common sites of infarction are the

Fig. 244.—Necrosis of Muscle-fibres of Heart (the pale area), resulting from thrombosis in a branch of the coronary artery. × 300.

anterior wall of the left ventricle near the apex, and that part of the anterior wall immediately adjoining the ventricular septum. More rarely, it occurs in the posterior wall, and almost never in the right ventricular wall. If death does not occur immediately, the muscle, at first reddish, soon undergoes necrotic changes, and becomes pale-yellowish in colour and soft in consistence. This softened condition, called by Ziegler **Myomalacia cordis,** may also be hæmorrhagic, and the area so affected is commonly surrounded by a zone of hyperæmia; and there is usually peripheral infiltration with leucocytes. At a later period, the muscle-fibres, on microscopical examination, are seen to be homogeneous in appear-

ance, their nuclei having lost the power of taking on nuclear stains; and a progressive formation of fibrous tissue, invading the area and replacing the muscle-fibres, takes place. This softened area, which has lost its contractility, may become stretched by the pressure of the blood within the heart, and **aneurism of the heart-wall** may thus be produced. The inner layers of muscle immediately under the endocardium may not be affected. If, however, they also become necrotic, **thrombosis** is liable to occur in the cavity, the thrombus becoming more or less adherent to

Fig. 245.—Anourism of the Heart. Thrombosis has occurred in the cavity of the aneurism, which is situated in the septum near the apex. (Edinburgh University Anatomical Museum. Catalogue No., Cir. C. c. 4.)

the surface of the infarct. If the infarct be small, complete absorption of the muscle-fibres, and their replacement by fibrous tissue, may be the ultimate result. If the vascular degeneration leads to prolonged mal-nutrition of the heart, gradual atrophy and degeneration of the muscle-fibres, and their replacement by fibrous tissue, take place. The patches of fibrous transformation vary in dimensions, according to the size of the artery obstructed. If this so-called **Fibroid Degeneration** be extensive, an irregular bulging or **Aneurism of the Heart-Wall** may be produced.

Microscopically, there may be merely diffuse masses of well-formed fibrous tissue, replacing the muscle-fibres; or, in other parts, the atrophied muscle-fibres are surrounded by, and enclosed in, the fibrous tissue.

ANEURISMS OF THE HEART.—As already stated, aneurisms of the heart are primarily caused by a degeneration of the muscle-fibres and their replacement by fibrous tissue. This newly-formed fibrous tissue stretches with the diastole of the heart, but, being non-contractile, it does not return to its normal condition during systole; and thus, the contractile force of the rest of the muscle, being transmitted by the blood and acting upon this weakened area, gradually produces a distinct bulging of the heart-wall.

If the area of fibrous transformation is a large one, this aneurismal bulging soon becomes pronounced, and gradually increases in size. These aneurisms are more or less globular in shape, and are practically always confined to the left ventricle, especially to its anterior wall at or near the apex. More rarely, they may be found in the ventricular septum. A much less common cause of aneurism of the heart-wall is the extension of an aneurismal dilatation in one of the valves, e. g. the mitral, and secondary involvement of the wall of the heart.

INFLAMMATION :--

(a) **ACUTE NON-SUPPURATIVE MYOCARDITIS** generally arises by direct spread of the inflammatory process from the **pericardium** or from the **endocardium.** In the instances in which it follows acute pericarditis, the condition may be wide-spread; whilst in those resulting from an endocarditis, the lesion is usually a localised one. Acute myocarditis may occur during the course of an acute infective disease, e. g. in typhoid fever, in diphtheria, in scarlet fever, in acute rheumatism, and other similar infections. These so-called **simple** forms of myocarditis usually occur in irregular areas, and are caused probably by the toxins rather than by the bacteria themselves. **To the naked eye,** the affected muscle-fibres are paler than normal, shew a reddish mottled appearance, and minute, opaque necrotic patches may be seen; but, in many cases, where, on microscopical examination, myocarditis is found, there are no obvious naked-eye changes. **On microscopical examin-ation,** cloudy swelling and other forms of degeneration are present, and the muscle-fibres are separated from one another by dilated and engorged capillaries, and inflammatory exudate which is largely cellular in char-acter. The cells may be of the polymorphonuclear, or, more-commonly, of the lymphoid, type, and there may be also evidence of proliferation of the connective-tissue cells of the part. Hæmorrhages into and between the muscle-fibres is sometimes seen, and the muscle-fibres themselves often shew necrosis. Complete **resolution** may take place, but, usually, areas of well-formed fibrous tissue remain as evidence of a former acute change. The heart-chambers, especially the left ventricle, in the walls of which the myocarditis is present, frequently become **dilated.**

(b) **ACUTE SUPPURATIVE MYOCARDITIS** is practically always associated with a septic embolism of the coronary arteries, and is part of a

general pyæmic condition. It may occur in **puerperal sepsis,** but it perhaps more frequently follows an **acute periostitis** or **osteomyelitis.** It may also be secondary to **ulcerative endocarditis.** **Abscesses,** varying in number and in size, some of them being microscopic in dimensions, are formed in the heart-muscle, especially of the left ventricle near its base and anterior surface. The abscesses are surrounded by a zone of congestion; and hæmorrhage may take place into or around them. **On microscopical examination,** fatty and necrotic changes are seen in the muscle-fibres, and collections of various forms of leucocytes, and, sometimes, the causal bacteria, are found in and between the fibres. If the abscesses are near the surface of the heart, they may rupture into the pericardium and give rise to **suppurative pericarditis;** or they may burst inwards through the endocardium.

(c) **CHRONIC MYOCARDITIS—FIBROSIS.**—In this condition, there is an overgrowth of fibrous tissue, not only between the muscle-bundles, but also replacing the atrophied and degenerated muscle-fibres themselves. This new formation of fibrous tissue interferes with the nutrition and causes further atrophy of the muscle, and thus fibrous patches of varying size, either localised, or scattered irregularly throughout the myocardium, are produced. This condition is most commonly found in the anterior wall of the left ventricle near the apex, in the septum, in the tips of the papillary muscles, and in the columnæ carneæ. The newly formed tissue may be cellular and shew only masses of lymphocyte-like cells and proliferated connective-tissue corpuscles; but, as a rule, it consists of well-organised and fully-developed fibrous tissue. This fibrous transformation of the myocardium is often described as **Fibroid Heart** or **Fibroid Degeneration of the Heart,** but, under these terms, are included various conditions, somewhat similar in character, though due to different causes. The principal of these are :—

(i) That form of fibrous-tissue overgrowth which is dependent upon **degenerative changes in, or obstruction of, the coronary arteries.** Thus, after infarction of the heart (*see* p. 524), there may be replacement of the necrotic muscle-fibres by fibrous tissue, which is in reality scar-tissue. More commonly, however, the fibrous transformation in the myocardium is a purely degenerative process resulting from an impaired blood-supply and consequent mal-nutrition, the more highly functioning muscle-fibres degenerating and being replaced by the less specialised fibrous tissue. Microscopical examination shews that the fibrous tissue is irregularly scattered, and para-arterial in its distribution—*i.e.* it is not immediately round the vessels but at some distance from them. The peri-arterial muscle-fibres are intact, and little islets of muscle, often shewing more or less marked degenerative changes, are thus seen embedded in the fibrous tissue. The fibrous tissue adjacent to the muscle is often very cellular, while that farthest away has a hyaline appearance.

(ii) **A purely degenerative change,** seen in old age in those cases where

the vascular degeneration is not a marked feature. In such conditions, the papillary muscles and the columnæ carneæ of the left ventricle are the principal, and may be the only, parts affected. This is not uncommon in wasting diseases—even in children.

A similar condition is seen in cases where there has been long-standing hypertrophy and dilatation of the right ventricle.

(iii) The interstitial overgrowth which is a **sequel of acute myocarditis,** and really, therefore, the result of the ordinary process of repair. In this somewhat rare variety, the new formation may be regarded as **scar-tissue,** and is peri-arterial in distribution.

Fig. 246.—Interstitial Myocarditis. The muscle-fibres have, in large part, disappeared and have been replaced by a moderately cellular connective tissue. ×75.

Aschoff and Tawara,[1] and, later, Coombs[2] and others, have described a form of myocarditis found in rheumatic hearts, which they regard as a sequel of **acute rheumatism.** This form of myocarditis is characterised by the presence of small "**submiliary**" **nodules** and areas of leucocyte-infiltration. The areas are rounded or fusiform, and formed by large spindle-shaped cells, lying in the inter-muscular trabeculæ of connective tissue. The nuclei of the cells are often multiple and do not stain intensely, though the cytoplasm of the cells stains deeply and uniformly. These large cells lie loosely packed in a fine fibrillary matrix composed of fibrin, and, surrounding them, are found leucocytes chiefly of the

[1] Aschoff and Tawara, *Brit. Med. Jour.*, 1906, vol. ii. p. 1103.
[2] Coombs, *Quarterly Jour. of Med.*, 1908, vol. ii. Nos. 5, p. 26, and *Jour. Path. and Bact.* Camb., 1911, vol. xv. No. 4, p. 489.

mononuclear type. The nodules are very often immediately related to arteries, and, according to Coombs, appear to arise usually from the peri-arterial connective tissue, or from the tunica adventitia of the artery itself. The nodules are found both in the subepicardial tissues and in the central parts of the myocardium, particularly in the wall of the left ventricle at the origin of the aorta, at the apex close to the septum, and at the attached margins of the mitral valve. They are less abundant in the right ventricle and in the inter-ventricular septum, and are comparatively rare in the auricular walls. These nodules appear to be stages in the production of a scattered myocarditis, which, at a later period, is demonstrable as irregular fibrous nodules or cicatrices. Whether these nodules are specific of acute rheumatism, as Aschoff and Coombs suggest, is not definitely established. They state that they are not usually found in non-rheumatic hearts and that they have been found in animals experimentally inoculated with streptococci from rheumatic cases.

Leucocyte-infiltration, lymphocytic in character, is certainly found in the myocardium in the majority of infective diseases, but the nodules so produced are small and, so far as our experience goes, they do not correspond with the submiliary nodules described by Aschoff and Coombs. Nodules more like those described by Aschoff have been recorded as occurring in cases of diphtheria.

Peri-arterial fibrosis occurs very rarely as a pure condition and is generally associated with a varying amount of the **para-arterial** type.

(iv) **Syphilitic Myocarditis.**—Syphilis is an important cause of interstitial myocarditis and of **Heart-Block,** which is more fully dealt with on p. 534. In some cases, there is definite **gummatous formation,** and, round this, a considerable amount of new fibrous tissue has developed. Sometimes, similar localised areas of new formation without a gumma are seen. Some authorities regard these as syphilitic in character, but there is no definite evidence on this point. Again, **syphilitic endarteritis** of the coronary arteries may cause degenerative changes in the myocardium, with overgrowth of fibrous tissue.

(v) **Tuberculous Myocarditis,** giving rise to chronic fibrous overgrowth with typical giant-cell formation. This occasionally occurs in the walls of the left ventricle, and the septum may also be extensively infiltrated.

§ HYPERTROPHY AND DILATATION :—

Hypertrophy and **dilatation** of the heart are conditions which are very frequently associated with one another. The hypertrophy of the muscular substance is, in many cases, compensatory in nature, and occurs because of some extra strain thrown on the heart. The same cause may give rise to dilatation, and, in some cases, it would seem as if the dilatation were the primary condition, and that the hypertrophy were the consequence. Frequently, however, the dilatation is a sequel of muscle-exhaustion in a hypertrophied heart.

This intimate connection between the two conditions makes it con-venient to study them together.

Ætiology.—Apart from the effects of **valvular lesions** in producing hypertrophy and dilatation of the heart (*see* pp. 514 *et seq.*), there are many other causes, some of which act on the heart as a whole, whilst others act on special chambers.

(1) **On the heart as a whole.**—Adhesions, not only between the epi- and peri-cardium, but also between the pericardium and the pleura or chest-wall, cause the heart to work under considerable difficulties, and are, therefore, one of the most certain causes of hypertrophy. Some of the largest hearts on record (*cor bovinum*) have resulted from this con-dition. The adhesions result from **pericarditis,** or from that condition plus mediastinitis and pleurisy; and, in some cases, the pericarditis is associated with valvular disease.

Minor degrees of hypertrophy are produced by prolonged over-stimula-tion of the heart, and the enlargement of the heart during pregnancy is probably to be explained on the ground of temporary extra strain. Excessive muscular exercise also leads to hypertrophy, and is common in athletes and in men doing heavy muscular work. Very frequently, this general hypertrophy is associated with dilatation, and the relative degrees of hypertrophy and dilatation will depend, to a certain extent, on the previous state of nutrition of the heart-muscle. If the muscle is degenerated, dilatation, rather than hypertrophy, will be the result of overstrain; whereas, in healthy muscle, if the strain is gradually applied, hypertrophy is the common result.

(2) **Localised to one or more chambers.**—This is very common, and may be associated especially with **Bright's disease,** with **valvular diseases of the heart,** and with **disease of the arteries, lungs,** and **pleura.** In **Bright's disease,** the **left ventricle** is specially affected, and the change is probably mainly due to the increased arterial tension produced by the products, normal or abnormal, of the retained urinary secretion, the heart having to drive the blood through the tonically-contracted peripheral arterioles. The hypertrophy may occur rapidly, *e. g.* in from eight to twelve weeks. The condition is generally a pure hypertrophy (**concentric hypertrophy**), unaccompanied by dilatation (*see* fig. 247). There is, owing to the con-tinuity and arrangement of the muscular fibres and to over-working of the whole heart, usually some associated hypertrophy—very-frequently with considerable dilatation—of the **right** side. The hypertrophy and dila-tation produced by **valvular diseases** have already been referred to, and need not be discussed further.

Chronic degenerative and other forms of **arterial disease,** and especially the diffuse form of arterio-sclerosis, by narrowing the lumen of the arteries, increase the work of the left ventricle, and may cause hyper-trophic changes in the myocardium of that chamber. Continued **excessive exercise** or severe muscular work, which act on the heart as a whole, cause special hypertrophy of the left ventricle.

Diseases of the lungs, such as emphysema, interstitial pneumonia of arfy variety, or **diseases of the pleura,** as for example pleural adhesions, may give rise to hypertrophy of the muscular wall of the right ventricle. This hypertrophy is very commonly associated with dilatation.

Hypertrophy and dilatation of the auricles alone are almost always the result of cardiac valvular disease.

Pathological Anatomy.—In **general hypertrophy** of the heart, the normal shape is not much altered. There is an enlargement of all the chambers, so that the heart may resemble that of a bullock (*cor bovinum*). **When the left ventricle is mainly affected,** the organ is increased in length and is more pointed than normal. The apex extends further to the left—so that the apical region appears to be specially prolonged. **On section,** the walls of the ventricle and the septum are markedly thickened, the septum often bulging into the right ventricle. This is specially well seen in transverse section (figs. 239 and 247), the chamber of the right ventricle, in such a section, often appearing as a crescentic slit-like opening.
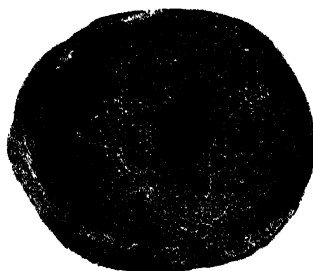
Fig. 247.—Transverse section through ventricles near apex, to shew "*concentric hypertrophy*" *of left ventricle* in Bright's disease.

Microscopically, there is an increase, both in number and in thickness, of the individual muscle-fibres. **When the right ventricle is hypertrophied,** the organ assumes a somewhat quadrilateral shape, its apex is obtuse, and the transverse measurement is increased. The right ventricle occupies almost the whole of the anterior aspect of the heart. **On section,** the wall is hypertrophied and the cavity is usually dilated.

GRANULOMATA, NEW GROWTHS AND PARASITES :—

Tuberculosis is very rare, but may occur in the form of minute granulations, though sometimes larger nodules are found. These nodules may extend to the pericardium and set up a tuberculous pericarditis. Tuberculous myocarditis has been referred to on p. 529.

Syphilis.—**Gummata,** though rare, occur in the heart-muscle (*see* figs. 248 and 249) and may give rise to very extensive nodular infiltration, or merely to small granulomatous or fibrous nodules. If they invade the conducting fibres or primitive muscle-tissue of the heart, they may give rise to the phenomenon of **Heart-Block** (*see* p. 534). Reference has

already been made to syphilis as a cause of vascular disease and of interstitial myocarditis (p. 529).

Primary Tumours very seldom occur, but **sarcomas, fibromas, lipomas, myxomas,** and **myomas** have been described both in the muscle and on the valves. The **Congenital Rhabdomyomata** which are found in the
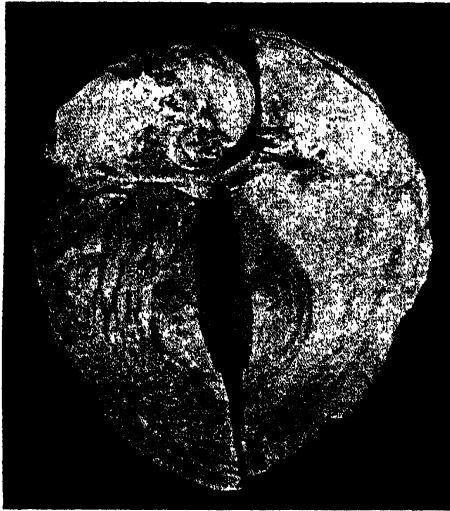
Fig. 248.—Large Syphilitic Gumma in the posterior wall of the heart. (Specimen lent by the late Professor Greenfield.)
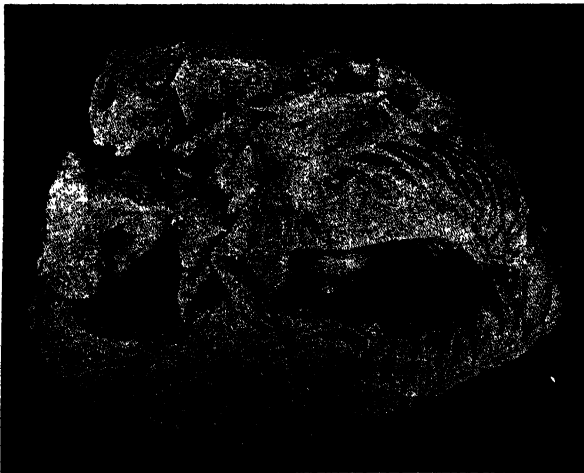
Fig. 249.—Syphilitic Gummata, causing obstruction of the tricuspid orifice. (Specimen lent by the late Professor Greenfield.)

myocardium are described under **Tumours** (see p. 299). They are found especially in certain cases of congenital idiocy, associated with tuberous (tuberose) sclerosis of the brain, adenoma sebaceum, and congenital tumours of the kidneys and other organs.[1]

[1] Fowler and Carnegie Dickson, " Tuberous (tuberose) Sclerosis," *Quart. Jour. of Med.,* October 1910.
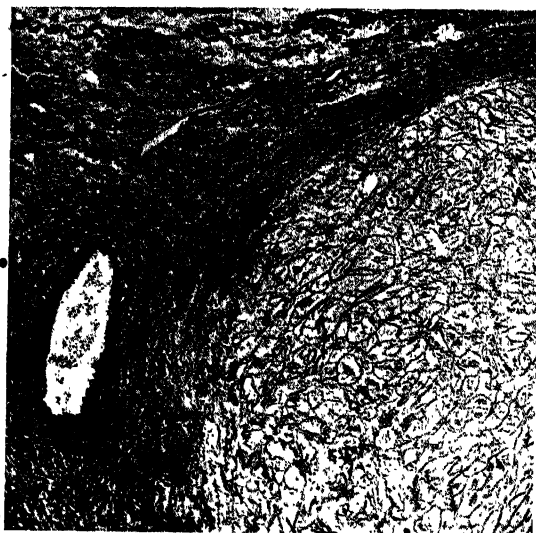
FIG. 250.—*Congenital Rhabdomyoma of Heart*, from. Fowler and Carnegie Dickson's case of tuberose sclerosis. Edge of nodule in wall of right auricular appendix. The tumour consists of a loose network of irregular, branching, striated muscle-cells. ×50.

FIG. 251.—*Congenital Rhabdomyoma of Heart*, from right auricular appendix of Fowler and Carnegie Dickson's case of tuberose sclerosis, shewing the large, extremely irregular tumour-cells, with irregular, striated fibrils. × 450.

Secondary Growths of melanotic sarcomas, lympho-sarcomas, and carcinomas, though comparatively rare, may occur.

. Hydatid Cysts have been found in the heart-wall.

HEART-BLOCK.—Anatomical and histological investigation has shewn that, at various areas in the heart, peculiar systems of muscular fibres exist. These are regarded as remains of the primitive musculature, and Keith holds that the greater part of the tissues of the auricles and the ventricles are outgrowths from the primitive cardiac tube, and that, in the auricle, the later developed muscular tissue has spread over the primitive remains, covering or displacing them. Portions of this primitive tissue, in isolated masses, are found, at the junction of the right auricle with the superior vena cava (the **sino-auricular (S.A.) node),** in the vicinity of the coronary sinus, in the valve of Eustachius, and at the mouths of the pulmonary veins. The muscle-tissue joining the auricles and ventricles probably belongs to the same system.

According to Lewis [1]:—" The special muscle-system (the **sino-auricular node**) lies at the junction of the free border of the appendix with the superior caval termination, and extends downwards along the sulcus terminalis for a distance of about 2 cms. in man. In thickness it is approximately 2 mm. The muscular fibres are small, being but a half or a third of the breadth of those of the auricular fibres proper. These fibres are striated, fusiform in shape, and are embedded in dense connective tissue."

Of the auriculo-ventricular connection Lewis gives the following description, which is founded on the work of Tawara :—

" The fibres of the junctional tissues may be traced from auricle to ventricle without break. The system commences in the auricle in the neighbourhood of the coronary sinus and at the base of the auricular septum, where a collection of the auricular fibres ultimately joining a specialised structure, the auriculo-ventricular node, is to be found. The node lies at the very edge of the auricular tissue at the posterior and right border of the septum. The bundle proper commences at the node, running almost horizontally forwards and to the left, ensheathed and isolated in a fibrous canal, and pursuing a course directly to the right of the central fibrous body of the heart to the *pars membranacea septi* of the ventricle. At the anterior part of this membrane the bundle divides, and the point of division lies a little in front of the anterior end of the attachment of the median or septal segment of the tricuspid valve to the ring. The left division of the bundle perforates the membrane, still lying ensheathed upon the upper border of the muscular septum, and enters the subendocardial space of the left ventricle at a point immediately beneath the union of the anterior and right posterior cusps of the aortic valve. Its further course is downward, and it may be traced under the endocardium of the septum of the left side. The right branch takes a sub-endocardial position directly after the division and, coursing downwards, enters the moderator band, or its representative, and proceeds directly to the papillary muscles, where it commences its arborisation. The arborisation of the left division starts upon the septum, and the main branches flow to the papillary muscles of the mitral valve. The arborisation on the right and left side is directly continuous with the extensive and complex subendocardial network of Purkinje fibres, which lines the greater part of the interior of both ventricles. From this network direct communication with the ventricular muscle fibres takes place. The smaller ramifications and strands of the network are

[1] Lewis, *Mechanism of the Heart-Beat*, London, Shaw & Sons, 1911.

frequently carried across the valleys between the muscular trabeculæ by means of bridges completely enwrapped by endocardium, and these bridges are conspicuous-at the apex of the left ventricle in almost every heart, be it human or otherwise.. It is said that the bundle and its branches are isolated by connective tissue beneath the endocardium until the papillary muscles are reached, and that no union takes place with the ventricular musculature during the earlier parts of the distribution; for no such union has been found up to the present time.

" The junctional tissues may be divided for purposes of histological description into the following portions :—

1. The auriculo-nodal junction.
2. The auriculo-ventricular node.
3. The bundle proper.
4. The right and left branches of the bundle.
5. The arborisations and the network of Purkinje.
6. The transitional fibres between network and ventricular substance.

" The histological structure of these several divisions varies considerably from one species of animal to another and the most marked differentiation is seen in the hearts of the ungulates. Yet there is much which is held in common. The following description applies particularly to the condition in the dog and in man in which the resemblance is close.

" The auriculo-nodal junction consists of fibres which are smaller than those of the auricle itself and which are arranged mainly in parallel fashion; the transition to nodal tissue is abrupt, and here the tenuity of the individual fibre is remarkable. The node consists of an intricate interlacement of the slender fibres, which cross and join at all angles. The fibres tend to be of spindle form and they are held apart by a rich network of connective tissue. Nerve fibres and ganglionic cells are scattered profusely amongst them in many hearts.

" The fibres of the bundle proper have a more parallel arrangement (they are chiefly parallel in man) and are stouter; they continue to increase in size as they are traced from bundle to arborisation and network, where they assume the proportions well known and characteristic of the fibres of Purkinje. They appear swollen, striation is comparatively sparse, the nuclei are large, pale and frequently multiple. According to Tawara, the transition to the ventricular musculature is abrupt and consists in a rapid decrease in size with a corresponding increase in striation.

" Thus in the course from auricle to ventricle there is at first a diminution in fibre size (which is extreme at the node), and increase in size (which is extreme in the network) and a subsequent and final decrease. The level at which the transition to the Purkinje type occurs is very variable in the different species; but this type is usually well represented in the fibres of the main branches.

" The network of Purkinje and the two main branches of the bundle may be readily followed with the naked eye in the freshly opened ventricles of the sheep and calf, and often in the human heart; a short dissection reveals the bundle itself, and it may be traced with ease to the tissues of the auricle.

" From the node in the wall of the right auricle, the bundle passes towards the ventricular septum, below the membranous portion of the septum, and divides into right and left branches—the right branch passing downwards in the septal wall of the right ventricle and the left passing through the ventricular septum to the wall of the left ventricle.

" The bundle in man and the sheep is from 1 to 2 mm. in thickness, and its fibres are conspicuous on account of their pallor.

" According to the modern view, it is by means of this bundle that the functional union of auricle and ventricle is effected, and it is through this structure that the impulses from the auricle, which initiate the ventricular contraction, are conveyed. They must, therefore, pass from the neighbourhood of the coronary sinus to the right and left groups of papillary muscles."

From the experimental side, it has been shewn that complete division of the auriculo-ventricular (**A.V.**) bundle produces complete heart-block; whereas, partial transection may produce little effect or only partial or temporary heart-block. These experiments lead to the conclusion that this auriculo-ventricular bundle is the essential organ of conduction, and, though certain experimenters have recorded contradictory results, yet the weight of evidence is in favour of this conclusion. At the same time, partial, or even complete, heart-block may result without any actual demonstrable destruction of these conducting fibres. It may be produced by stimulation of the vagus nerve, by the injection of digitalis, aconitine, adrenalin, muscarine and physostygmine, and it may result from the cardiac poisoning of asphyxia. It has been suggested as an explanation, that the junctional tissues have a peculiar susceptibility to the influence of certain cardiac poisons.

Careful *post-mortem* examinations have been made in cases of heart-block, but from these it is difficult to draw very definite conclusions, because the lesions which have been found are usually wide-spread, and, though they involve the primitive tissues, yet they are not confined to these special areas. At the same time, an analysis of the recorded cases shows that, in the great majority, there are definite pathological lesions affecting the conducting bundles, and these lesions may be of the nature of **gummata, fibrosis** with or without calcification, **chronic inflammatory lesions, ulceration, parenchymatous** and **fatty degenerations,** and the changes resulting from **acute** and other forms of **rheumatic inflammation.** In rheumatic affections, and particularly in the case of patients with advanced mitral stenosis, impaired conduction is frequently manifest. Careful histological examination, in such cases, will generally reveal the presence of diffuse fibrosis, lymphocytic infiltration, and other chronic inflammatory changes, particularly in the sino-auricular node and in the auriculo-ventricular node and bundle. Poisoning with digitalis produces heart-block in experimental animals, and Mackenzie has shown that a certain degree may be produced in man by this drug, even in medicinal doses, in hearts the conducting bundles of which have been impaired by an attack of rheumatism. Possibly the digitalis acts indirectly through the vagus nerve.

In **paroxysmal tachycardia, auricular flutter** and **auricular fibrillation,** no distinct pathological conditions have been found. Cowan states that these clinical phenomena may occur in both sexes and at every age, in every form of organic disease and in hearts that are apparently normal. When they occur frequently or are permanent, they are probably always a sequel to organic disease.

DISEASES OF BLOOD-VESSELS

Anatomy.—In all parts of the vascular system there is a lining of **endothelial cells,** and a slight amount of **connective tissue** (fibroblasts and fibrils), on which this endothelium rests. In certain vessels, and particularly in the arteries, there is either a definite **elastic lamina** or **scattered elastic elements** lying external to the connective-tissue layer already noted. External to this elastic layer, or intermingled with it, there is a greater or less amount of **smooth muscle-cells and fibrous tissue.** The intima and the adjoining part of the media contain no capillaries, and are, therefore, nourished by the blood circulating in the vessel. External to this, the vessel-wall is nourished from the vasa vasorum, and, in the outer coat (adventitia), which, in the majority of arteries, is composed of connective tissue, there is a rich system of perivascular lymphatics. In certain vessels, e. g. the external iliac and the renal, as pointed out by Andrewes [1] and Gaskell, a thick layer of longitudinal muscle-fibres is sometimes found in the adventitia.

In studying diseases of vessels, it must be remembered that, though the whole vascular, and especially the whole arterial, system is subjected to **constant strain,** the effects may be either **general** or merely **local.** The results themselves and their distribution or localisation depend on various factors. The general condition of the surrounding tissues may play a very important part. Where the vessels are **imperfectly supported,** dilatations more readily take place; and, if the surrounding tissues undergo retrogressive changes, the vessels may share in these degenerations. The **nutrition of the wall** of the vessel is of extreme importance. In the smaller and medium-sized vessels, resistance to strain depends mainly on the muscular coat; but, as the vessels increase in size, more and more elastic tissue is developed in their walls, and this increases their resiliency and power of resisting dilatation. Therefore, anything interfering with the nutrition of the muscular and elastic tissue will increase the tendency to degenerative changes. Again, the nutrition of the vessel depends—perhaps to a larger extent than does that of any other organ or tissue—upon the condition of the blood flowing through it, the inner coat being nourished wholly by the blood with which it is in contact. An impoverished condition of the blood, or the presence in it of toxic and irritating substances, will act with special severity on the vascular system. Experiment seems to show that certain toxic substances, when present in the blood, produce thickening of the inner coat of the vessel, whilst others act specially by causing degenerative changes in the media. If the inner coat becomes much thickened, the nutrition of its deeper part is interfered with, and degenerative changes are liable to occur there. Further, the toxic substances may act by causing spasm or dilatation of the vessels: or by altering the " selective " capacity of, or by bringing about degenerative changes in, the endothelium. Proper nerve-control of the vessels is essential to a healthy condition of their walls.

In studying the pathological conditions of the blood-vessels, careful consideration should be given to the following changes :—

1. Those which are produced **from outside,** by gunshot and other wounds, not necessarily opening into the vessels, by an alteration of the surrounding tissues, by tumour-growth or by inflammatory or proliferative conditions, such as are seen in wound-healing. Thus, the vessels may be pressed upon, and their lumen partially or completely obliterated;

[1] Andrewes, *Report on Arterial Degeneration and its Premature Occurrence* (Report of the Medical Officer to the Local Government Board, Appendix B, No. 1, 1911–1912).

or *they may share in the proliferative changes, and obliteration may be* brought about in this way.

2. Those which result from spasm or dilatation, or from injury to, and degenerative changes in, **the wall of the vessel.**

3. Those which are produced **from within,** by alterations in the condition of the blood or the presence in it of toxic substances, by embolism, by increased blood-pressure, etc.

4. Those which are due to **alterations in nerve-control.**

(A) DISEASES OF SMALL VENULES AND CAPILLARIES

The **venules and capillaries** may undergo **hypertrophy** and **thickening** as a result of long-standing **strain.** This condition is well seen in the capillaries of the lung, and in those of the glomeruli in the kidney, in cases of long-standing **venous obstruction.** This hypertrophy or thickening is shown, microscopically, by the presence of a more or less well-developed layer of fibrous tissue external to the endothelium, and it seems probable that this is produced by the hypertrophy of a pre-existing, and, it may be, very delicate peri-endothelial (perithelial) layer of fibrous tissue.

DEGENERATIVE CHANGES such as **cloudy swelling** and **fatty degeneration** are very common in the endothelial cells of the venules and capillaries in conditions which give rise to these alterations in other organs and tissues. **Hyaline degeneration** in the glomerular capillaries in the kidney, and in the vessels in the spleen and other organs, is common in scarlet fever, diphtheria, and certain other diseases. **Amyloid** or **waxy degeneration** is very often observed in the supporting connective tissue of the capillaries. **Pigment,** taken up by the endothelial cells, which are actively phagocytic, is seen in cases of malaria.

(B) DISEASES OF ARTERIES

INJURIES.—Apart from the damage which may take place in any artery in an open wound, there may be bruising of the vessel without any obvious opening into it, in gunshot wounds, etc. In such cases, **circumscribed hæmatomas,** or even traumatic aneurisms, may appear some time after the injury—the former being due apparently to a rupture, and the latter to a distension, of the bruised and weakened vessel-wall.

ATROPHY of arteries may take place in a part of the body which has become, or is becoming, functionless, *e. g.* in the femoral and other arteries after amputation through the thigh, or in arteries supplying glandular structures which are undergoing, or have undergone, involution.

HYPERTROPHY or simple increase in the size of the lumen and walls of vessels occurs when a collateral circulation develops after obstruction of a larger artery; and hypertrophy of the muscular coat may occur in some affections, *e. g.* in Bright's disease.

•DEGENERATIVE, INFLAMMATORY, AND PROLIFERATIVE CHANGES

(a) **FATTY DEGENERATION.**—This occurs especially in the **intima** of the smaller arteries, and in that of the aorta and its larger branches; whereas, in the medium-sized arteries, it is perhaps commoner in the **muscular coat.** The change in the intima is due usually to disturbances of the circulation or to the presence of toxic substances in the blood; that in the media is most commonly a sequel of atrophic or senile alterations; and both are frequently followed by calcification. The degenerated areas appear as raised streaks or irregular patches of a pale-yellowish
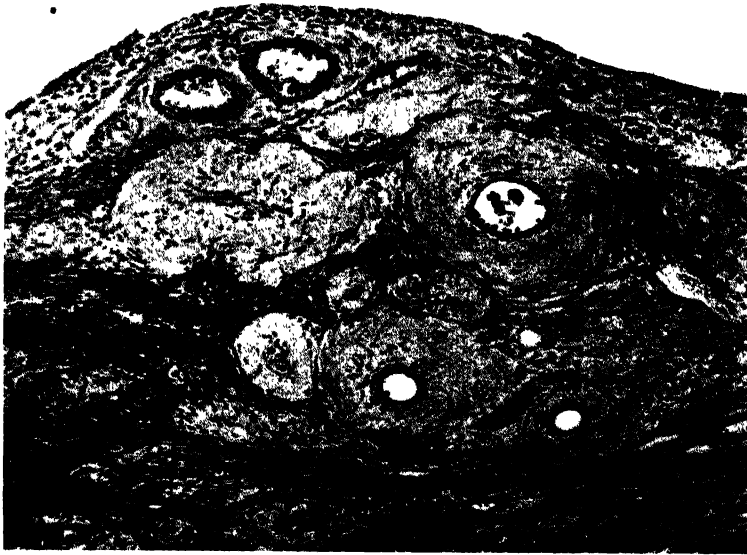
Fig. 252.—Hyaline Degeneration of Small Arteries in Ovary   × 120.

colour in the inner coat, and, **microscopically,** they are found to be composed of fatty granules in the endothelial cells, and also in and between the connective-tissue corpuscles, or in and between the muscle-fibres in the middle coat.

(b) **CALCAREOUS DEGENERATION OR INFILTRATION.**—This is commonly secondary to necrotic, fatty, or hyaline change, but it may occur as a primary condition in the middle coat, and, especially as a senile change, in some of the medium-sized or smaller arteries. The femoral, the brachial, the aorta at its bifurcation, the common iliacs, and some of the smaller arteries of the brain are among the commonest sites of this change. In the **primary** form, the granules, in almost all cases, appear first in the muscle-cells of the middle coat. They accumulate, forming irregular calcareous patches, which necessarily give increased rigidity to the walls of the arteries. This calcareous degeneration of the middle

coat is often associated with atheroma, but **these conditions should not be regarded as identical.**

(c) **HYALINE** and **AMYLOID** or **WAXY DEGENERATIONS** occur specially in the walls of the smaller arteries, and are fully described under **General Retrogressive Processes** (*see* Chapter II., pp. 28 *et seq.*).

(d) **ACUTE INFLAMMATION OF ARTERIES, ARTERITIS.**—Arteries may share in the acute inflammatory changes which occur in their neighbourhood, but a primary acute arteritis is very rare. Such an **acute arteritis** is almost exclusively confined to the inner coat of the large blood-vessels, especially the aorta near its commencement. The condition may result from the extension of acute endocarditis of either the aortic or pulmonary valves; and it occurs also as a result of severe syphilis, especially if associated with excessive alcoholism. In any type of acute arteritis, **thrombosis** is a common sequel. If sepsis is present, the thrombi undergo softening, and the **septic emboli** become impacted in the walls of smaller arteries, there setting up acute inflammatory and even suppurative changes. Ulceration or abscess-formation may be produced, and, on account of weakening of the vessel-walls, multiple acute aneurisms may develop.

Microscopically, the walls are seen to be infiltrated with leucocytes, the connective-tissue cells between the laminæ of the inner coat swollen and proliferating, and the muscle-fibres separated by inflammatory exudate and, it may be, undergoing necrotic changes. In the syphilitic cases, enormous numbers of spirochætes may be found. In the **suppurative** forms, definite abscesses are sometimes present.

(e) **THROMBOSIS** and **ORGANISATION OF THROMBI IN ARTERIES** are dealt with on pp. 137–143 and 219–220.

(f) **ARTERIO-SCLEROSIS.**—This term is now very commonly used by clinicians, and by some pathologists, as applicable to all forms of sclerosis or " hardening " of the arteries. We propose to include under the term those conditions in which the proliferative and degenerative changes are confined to, or are most marked in, the inner coat. Thus, we include both that form of proliferation and degeneration of the inner coat which is, by common consent, called atheroma; and also that thickening of the intima of arteries which is found in connection with atrophic cirrhosis of the kidney. In this latter condition, the proliferative changes are the more pronounced, causing, it may be, great narrowing of the lumen of the artery; whilst the degenerative changes may be very slight. On this limitation, much of the recorded experimental work on the production of arteriosclerosis, or, as we prefer to call it, atheroma, must be excluded, for, as the work of Klotz,[1] Rickett,[2] and others shews, the nearest parallel in human

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[1] Klotz, " The Experimental Production of Arterio-Sclerosis," *Brit. Med. Jour.*, December 22, 1906.

[2] Rickett, " Experimental Atheroma," *Jour. of Path. and Bact.*, October 1907.

(In these papers full references are given.)

pathology to the experimental lesions which have been produced by these observers in animals is **calcification of the media.** In some of the experiments by Klotz, in which the arterial lesions were produced by inoculation with *B. typhosus* and *Streptococcus pyogenes,* he records the presence of areas of thickening of the intima, with fatty degeneration of the subendothelial tissue : and splitting and fragmentation of the internal elastic lamina : together with proliferative connective-tissue changes invading the degenerating areas. He places these latter lesions "in very close relationship with arterio-sclerosis in man, as it is described by Jores," and states that: " if we are to accept Jores' definition of arterio-sclerosis, namely, that it is a disease consisting of a hyperplasia with degeneration of the musculo-elastic layer of the intima, as seen in the human aorta," the lesions most commonly produced by his experiments " would not fall in this category."

Cowan [1] describes **Arterio-sclerosis** as a diffuse affection, in which the **intima** is more or less thickened : the **elastic fibrils** hypertrophied at first, and later granular, and the connective tissue hyaline : the **media** at first hypertrophied, and, later, atrophied, and perhaps fatty, eventually being largely replaced by connective tissue : the **adventitia** invariably thickened and, in old-standing cases, hyaline. He states that the gross fatty and calcareous changes which occur in atheroma are rarely seen, and that the adventitial thickening is the only constant change in these cases. The medial hypertrophy he regards as an early and essential phase, but he believes that fibroid changes supervene at a comparatively early period.

We regard the terms **Arterio-sclerosis, Atheroma,** and **Endarteritis deformans** as practically synonymous; and, on this basis, the following description of the condition is founded.

Arterio-sclerosis, Atheroma (or **Athero-sclerosis,** as it is termed by recent German writers).—The essential lesion, in this condition, is a thickening of the intima, with varying degrees of degenerative changes in its deeper part, *i. e.* the part most distant from the lumen of the vessel. The thickening is, commonly, limited in area, producing irregular patches or flattened nodules; but it may be more diffuse and widespread, giving rise to general thickening and rigidity of the vessels. In the former variety, **nodular atheroma,** which is commonest in the aorta and large vessels, and, in the syphilitic variety, often confined to the arch, distinct elevated patches, with—to the naked eye, at all events—well-defined edges, are seen (*see* fig. 254). At first, these areas are translucent or pearly in appearance, but soon assume a dull white or yellowish colour, on account of the fatty degeneration which occurs in the deeper part of the patches. As they become older, they tend to increase in size, adjacent patches coalesce, the fatty degeneration becomes more marked, and lime-salts are deposited in the degenerated areas. Thus are produced large, irregular, raised,

[1] Cowan, *Diseases of the Heart*, Arnold, 1914.

calcareous nodules in the inner wall of the vessel (see fig. 254). The continuity of the endothelium covering the patches is at first preserved; but, at a later stage, this also undergoes degenerative changes and may become lost, and, as a result, thrombosis is very liable to occur on the roughened patches. The calcified plates crack across, and thus the blood in the vessel may burrow its way between the inner and middle coat, or between layers of the middle coat, and produce the condition of **dissecting aneurism.** The degenerated focus may soften completely, and form a cavity containing fatty débris and crystals of the fatty acids. The tissue superficial to the cavity may eventually give 'way and thus form an **atheromatous ulcer,** in the walls of which calcification occurs.

FIG. 253.—Radial artery, shewing an early patch of thickening of the intima (on the right). The elastic lamina is stained dark. × 28.

On **microscopical examination** (see Chapter II., Plate I., fig. 4), the change is seen to consist of a **laminated thickening of the inner coat,** due to proliferation of the subendothelial connective tissue, and perhaps also, as some writers believe, of the endothelium. In the early stages, many round, oval, or irregular cells are found between the connective-tissue strands. The thickening may be very considerable in amount. In its normal condition, the intima is nourished by the blood in the lumen of the vessel. When the inner coat becomes thickened

beyond a certain degree, its deeper part cannot receive sufficient nourish-
ment from the blood circulating in the lumen, and, unless it can obtain
its blood-supply from some other source, it degenerates.   This degenera-
tion is, at first, of the nature of a **fatty transformation,** or is partly necrotic
in character, and, at a later period, **calcification** takes place.   The **elastic
tissue** in the larger arteries may become fragmented, but there seems to be
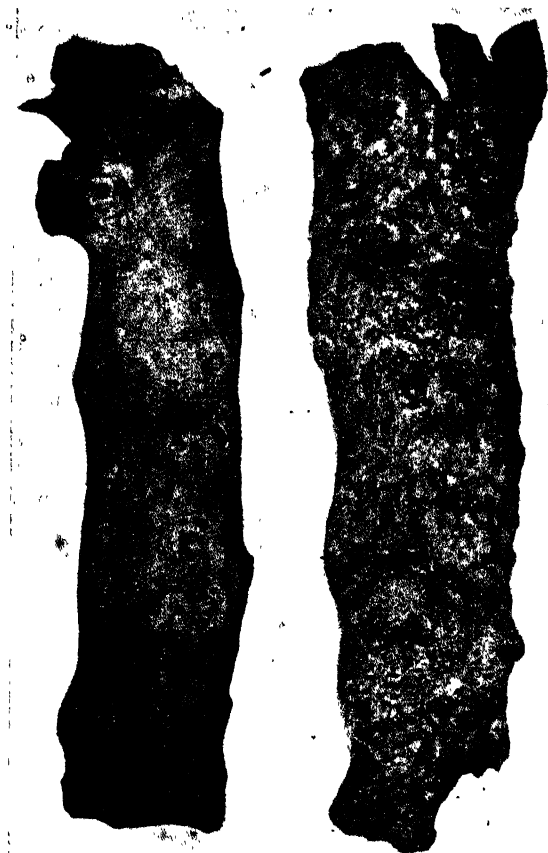
FIG. 254.—*Atheroma of Aorta.*   In one specimen the change is seen specially round the
orifices of the arterial branches; in the other it is more advanced and widely spread.

some evidence that an actual proliferation of it takes place.   In the
smaller arteries, the internal elastic lamina becomes straightened out
and fragmented, and, at places, it may entirely disappear.   The muscular
part of the **middle coat** may remain unaltered, but degeneration and
atrophy of the muscle-fibres, with an over-growth of fibrous tissue, espe-
cially opposite the site of greatest thickening in the inner coat, are of fre-
quent occurrence; and it is said that this secondary thickening is a marked
feature of the syphilitic type of the disease, if the process is not very

FIG. 255.—Aorta, shewing great thickening of intima with degeneration in its deeper part. × 30 diam.

FIG. 256.—Thickened Arteries in the Kidney, shewing increase in elastic tissue. × 200.

acute. There may be a deposit of lime-salts in the degenerated parts of the muscular coat; or, in some cases, myxomatous degeneration occurs; and the possibility of a new formation, not only of strands of elastic tissue, but of a definite elastic lamina, must be recognised. The **outer coat** may be unaltered, or a certain amount of fibrous hyperplasia be present in it. In the syphilitic cases, there is an infiltration of lymphocyte-like cells round the **vasa vasorum** both in the media and the adventitia.

In the diffuse or sclerous form of atheroma, the arteries are usually

FIG. 257.—Atheroma in a cerebral artery, shewing the thickening and degeneration of the intima, the fragmentation of the internal elastic lamina, and the degenerative changes in a portion of the media.   × 40.

dilated, and, on section, in spite of the thickening of the inner coat, remain abnormally patent, though, in some cases, this thickening may be so great as to cause complete obliteration of the lumen. The vessels may be tortuous—this tortuosity being due to their loss of elasticity and consequent elongation.

On **microscopical examination,** the thickening of the inner coat is usually more or less uniform, and is made up of regular concentric layers of fibrous tissue. Fatty and other degenerative changes may be found, but they are not so common as in the **nodular** form.

The middle coat is said by some authorities to be hypertrophied.

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We, however, are not prepared to accept this statement as applicable in all cases. Hypertrophy of the middle coat occurs in a certain proportion; but in others there is definite atrophy of the muscle-fibres; whilst in some, where there is apparent thickening, this is due, not to hypertrophy, but to overgrowth of fibrous tissue consequent upon atrophy of the muscular substance—a phenomenon which can be well demonstrated by such differential stains as van Gieson's picro-fuchsin. The internal elastic lamina may lose its wavy character, and is frequently swollen and fragmented. The outer coat sometimes shews fibrous overgrowth.

Sites of Occurrence.—The **nodular form** is seen especially in the aorta and large vessels. In the aorta, the condition is most marked in, and

FIG. 258.—Arteries in the Kidney from a case of chronic Bright's disease, shewing the regular laminated thickening of the inner coat. ×50.

may be confined to, the arch, in which the thickening and the degenerative changes are developed especially immediately above the valve-cusps and round the origins of the coronary arteries and the great vessels of the neck: though, in the syphilitic type of the disease, there may be no special relationship to the emergent vessels. When it occurs in the thoracic or abdominal aorta, the same advanced change is frequently seen round the origins of the intercostal, lumbar, and other arteries, and also especially at the bifurcation of the abdominal aorta into the common iliacs. The coronary arteries of the heart and the arteries of the brain may shew this degenerative condition in a more or less pronounced degree; and the pulmonary arteries may also be affected, especially in mitral stenosis, in which condition even the smallest visible branches of the vessel may shew the change. In the **diffuse** or **sclerous form,** the medium-sized and smaller

vessels, such as those of the kidneys, brain, or ovaries, are most commonly affected, and the change is best seen in the arteries of the kidney in cases of chronic Bright's disease. The thickening of the inner coat may be so marked as to cause complete, or almost complete, obliteration of the lumen of the vessel.

Ætiology.—It is extremely difficult to assign any definite causation for most individual cases of atheroma. It is so constant in old age, that a certain degree of it may be considered almost a physiological

Fig. 259.—Ovary : arteries shewing marked thickening of inner coat.   ×90 diam.

process; but, in younger people, it is known to occur as a sequel of syphilis, gout, alcoholism, and chronic toxæmias of any kind. Patches of early atheroma are frequently found immediately above the valve in the aorta of young children and even of infants. In certain cases of chronic nephritis, the arterial changes seem to be due to the non-elimination of effete and toxic products by the damaged kidney, but there is little doubt that, in many cases, the kidney-condition is a **sequel** of the vascular change. The experiments by Klotz, already referred to, appear to shew that atheroma may be produced by the direct action of bacteria or their products on the vessel-wall. The sites at which it occurs point specially

to friction or strain as being an important causal factor. Thus, in the aorta, *the condition is always most marked in that part of the arch which is most exposed to the impact of the blood during the systole of the heart*, and at the orifices of branches, where the friction and strain are also great. Again, in cases of congenital narrowing of the aorta, there may be very marked atheroma on the proximal side of the stricture, whilst the vessel-wall on the distal side may be quite unaffected with the disease. In the pulmonary artery, the condition is most marked in cases where there is increased pressure in the vessels, as, for example, in cases of chronic venous congestion arising from obstruction at the mitral orifice, combined with hypertrophy of the walls of the right ventricle.

McNee and Wilson [1] have shewn that, by feeding rabbits on **cholesterol** for from three to six months, there is produced, at first, a distinct **thickening of the intima** in the aorta: that this thickening is formed in irregular patches : and that, later, a **fatty** deposit is found in the deeper layers of the thickened inner coat. In some of their experimental animals, they found also **degeneration** and **calcification** in the media. These experiments, which are confirmatory of those carried out by Anitschkow and Chalatow,[2] have produced changes which approach very closely to those found in human arterio-sclerosis. Other observers have produced similar changes by feeding rabbits on purely animal food, *e. g.* ox-flesh, eggs, and milk. The liver, in these cases, becomes laden with droplets of fat which, on examination, are found to consist of doubly refracting cholesterol-ester fat. Further interest is given to those experiments when we consider that cholesterol is a normal constituent of every cell in the body, and that it is present in considerable amount (1·5 to 1·8 grammes per litre) in the blood-serum, chiefly as cholesterol-ester. This cholesterol-ester is found in the arteries in arterio-sclerosis, and in the kidney in chronic Bright's disease ; and in these and various other pathological conditions, it is markedly increased in amount in the blood-serum. The following is an analysis by Windaus [3] of normal and arterio-sclerotic aortæ :—

1. NORMAL AORTÆ

Free Cholesterol.	Cholesterol-ester.
A. 1·19	0·47
B. 1·03	0·32

2. ARTERIO-SCLEROTIC AORTÆ

Free Cholesterol.	Cholesterol-ester.
A. 4·49	3·75
B. 7·41	10·53
C. 6·73	7·92

The figures indicate grammes per 1000.

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[1] McNee and Wilson, *Communication to Pathological Society of Great Britain and Ireland*, June 1914.

[2] Anitschkow and Chalatow, *Centralbl. f. allg. Pathol. u. Path. Anat.*, Jena, 1913, xxiv. 1; also Ziegler's *Beitr. z. Path. Anat. u. allg. Pathol.*, Jena, 1913, vi. 379.

[3] Windaus, *Zeitschr. f. physiol. Chem.*, Strasburg, 1910, lxvii. 174.

In various forms of Bright's disease, the increase is from 2·5 to 4·2 grammes per litre of the blood-serum.

Further interesting facts on this subject are given in a paper by McNee.[1] The changes have been found in rabbits, but not in carnivora, and in the aorta, but not in the smaller vessels, and, therefore, definite conclusions cannot, as yet, be drawn from these experiments, though the work is extremely suggestive.

Pathogenesis.—The manner in which the various causes operate in producing arterial degeneration is still an unsolved problem. According to Thôma and others, the changes are due to the adaptation of the vessel to the diminished velocity of the blood-stream produced by the inability of the middle coat to contract, the amount of blood flowing through the vessel being mainly regulated by the calibre of the artery. They hold that there is a primary degenerative change in the muscular coat, which leads to a loss of its power of contraction. The vessel thus becomes dilated at these degenerated areas, and, in order to make up for this dilatation and slowing of the blood-stream, a compensatory thickening of the inner coat takes place. If the rate of the flow were reduced to one-half, the sectional area of the vessel, they believe, would be diminished to one-half, and the channel would be about half the normal. If this diminution cannot be brought about by muscular contraction, it will, they maintain, occur by a gradual fibrous thickening of the inner coat. This theory necessarily postulates some primary damage to the middle coat. Though this primary muscle-degeneration may sometimes occur, atheroma may be present in an artery the media of which is apparently quite healthy; and, moreover, in many cases, the change in the media is the **effect,** and not the cause, of the alteration in the intima.

The experimental work of Klotz, to which reference has already been made, shews that the thickening of the intima may be produced without any obvious change in the media, and, apparently, by the direct action of bacteria or their products on the intima itself; and, further, Klotz, Rickett, and others, have shewn that extensive degenerative changes in the muscular coat are not necessarily followed by proliferative changes in the intima.

The more commonly accepted view is that the thickening of the intima is the direct result of excessive pressure, or strain, or of the action of toxins upon the walls of the vessels, or of a combination of these; and that it is more liable to occur in vessels the elasticity of whose muscular coat is impaired by malnutrition or other cause. Increase of pressure in the vessels may bring about a loss of elasticity, and this probably explains why, in cases of muscular overwork, or in persons in whom the heart is hypertrophied, atheroma commonly occurs.

Effects of Atheroma.—The vessels may be considerably narrowed,

[1] McNee, *Quart. Jour. Med.*, April 1914 (vol. 7, No. 27).

and, if this happens in the smaller arteries, such as those conveying blood to the heart, the brain, the kidney, and the extremities, there may be marked nutritional changes in the areas supplied. Thus, in the **heart,** there may be some atrophy of the muscle-fibres and replacement of these by fibrous or fatty tissue; or, if the vessel becomes thrombosed—a likely result of the degeneration and narrowing—infarction and necrosis may occur. In the **brain,** softening is a frequent result of such narrowing of the arteries; and, in the **kidneys,** degenerative changes and overgrowth of fibrous tissue commonly occur.

The narrowing of the peripheral vessels constitutes an impediment to
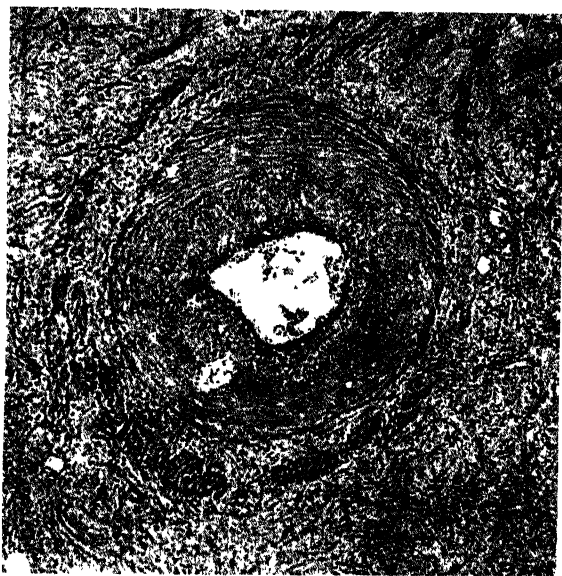
Fig. 260.—Thickened Artery from the stomach-wall in a case of chronic gastric ulcer. × 75.

the blood-flow, and hence to the action of the heart; and this leads to hypertrophy of its muscular walls, especially those of the left ventricle.

The rigidity and the loss of contractility and elasticity of the walls, produced by the atheroma, are very important factors in the causation of aneurism.

(*g*) **ENDARTERITIS PROLIFERANS OR OBLITERANS.**—This is a chronic process in which the main feature is a concentric thickening of the intima, without the occurrence of degenerative and necrotic changes in the proliferated tissue. The thickening may be so great that, in some instances, the lumen of the vessel is almost, or even completely, obliterated. The newly-formed tissue in the intima is vascular, and is really of the nature of granulation-tissue. This condition is well illustrated in the proliferative and obliterative changes which take place in the vessels

during **the healing of a wound,** and in **chronic irritative or inflammatory diseases** such as tuberculosis, leprosy, and syphilis (*see* figs. 260 and 261). It is also seen in cases of chronic Bright's disease and of silicosis. A somewhat similar appearance of the intima is produced during the organisation of thrombi.

(*h*) **SYPHILITIC DISEASE.**—Syphilis may affect the arteries in various ways. It is undoubtedly one of the causes of **atheroma,** especially in the aorta. In the smaller vessels, however, the condition produced is usually one of **endarteritis proliferans,** with or without proliferative changes in the outer coat. The essential lesion, in all cases, is the formation of young granulation-tissue, which, at a later period, undergoes transformation into well-formed fibrous tissue. According to most observers, the affections of the aorta caused by acquired syphilis are found especially in the ascending part of the arch; and, in early and more acute affections, the patches or plaques have a thick, raised, almost "fleshy" appearance, and are semi-translucent, pale, white, or slightly pinkish in colour. Later, when viewed from the intimal surface, they show a peculiar stellate scarring, with deep furrows and extensive endothelial proliferation. Calcification is not common. Microscopically, there is an abundant infiltration of lymphocyte-like cells (plasma-cells, etc.) following the distribution of the vasa vasorum, destroying locally the elastic and muscular elements of the media, and causing extensive gaps in this coat. These gaps are ultimately filled by fibrous tissue, and a thickening of the intima takes place over them.

The *Spirochæta pallida* is found, often in considerable numbers, in these areas in the media. The vasa vasorum may show endarteritis proliferans. Aneurismal dilatation is common and is explained by the marked degree of mesarteritis.

Syphilitic endarteritis is, according to Greenfield, most typically illustrated in the proliferative or obliterative form of the disease seen especially in the arteries of the brain. The change is usually wide-spread, but sometimes it may select one or, more frequently, a group or system of vessels in certain organs or tissues.

The inner coat becomes thickened by the formation of more or less regular, concentric laminæ of fibrous tissue, which may greatly narrow, or even obliterate, the lumen. Between the connective-tissue laminæ, elongated cells are found—the relative proportion between these two sets of structural elements varying with the rapidity or the chronicity of the change. If **rapidly growing** and in the **early** stage, the newly formed tissue is more cellular; if **slowly developed** and of some standing, more fully formed fibrous tissue is seen. In the process of formation of this new tissue, young, thin-walled capillaries are developed. These grow from the **vasa vasorum,** penetrate the internal elastic lamina, and vascularise, and so help to maintain the nutrition of, the newly forming tissue. It is on account of this vascularisation that degenerative changes, such as occur in the

nodular form of atheroma, are absent in this variety of endarteritis. The newly-formed tissue of the intima consists of actively developing granulation-tissue. According to many authors, the intimal proliferation is a process secondary to the medial change, but this, in our opinion, is not borne out by facts. We regard the intimal change as the result of a chronic inflammation caused by the poison of syphilis acting directly on the inner coat of the vessel, the *Spirochœta pallida* being found in this coat, though it is also present, as already stated, in the degenerated

Fig. 261.—Syphilitic Artery, shewing proliferative changes in the inner coat (endarteritis proliferans), and also peri-arteritis. ×30.

areas of the media. **The middle coat** may show some cellular infiltration, and also fibrous change when the condition is at all advanced. **The internal elastic lamina** is usually unaffected, but there may be an actual new formation of elastic tissue (*see* fig. 256). **The outer coat** generally shews active proliferative changes, with great accumulations of small lymphocyte-like cells, and the formation of granulation-tissue. This ·syphilitic peri-arteritis is seen especially around the small arterioles and vasa vasorum. The cellular infiltration may extend into the outer layers of the media, where the *Spirochœta pallida* is also found.

　　Effects.—Syphilitic disease—especially when it attacks some of the

larger vessels, *e. g.* the basilar and other cerebral arteries, carotids, aorta, cœliac axis, etc.—causes a loss of elasticity, and, as a result, dilatation takes place. This dilatation may be very irregular, and may lead to the formation of aneurisms; but aneurismal dilatation of the larger vessels may also be produced by syphilitic endarteritis causing obliteration of the vasa vasorum, the consequent loss of nutrition leading to degeneration and weakening of the wall of the large vessel.

The narrowing of the vessels may give rise to nutritional changes and overgrowth of fibrous tissue in the various structures to which they are distributed; or it may cause thrombosis in the vessel itself, just as do the changes in atheroma.

NOTE.—Russell,[1] who has done valuable work in connection with the diseases of arteries, has emphasised the confusion which exists, especially in English textbooks of medicine, since the introduction of the term arterio-sclerosis. He classifies " the pathological changes in arteries which are of practical importance to the clinician " thus :

    1. Atheroma and Endarteritis Deformans.
    2. Obliterative Endarteritis and Acute Aortitis.
    3. Calcareous infiltration of the tunica media.
    4. Arterio-sclerosis.

He places, under atheroma, only that variety which we have described as " nodular atheroma," including the " sclerous form " with obliterative endarteritis. We have no great objection to this, though we prefer the grouping which we have given, and which was for so long taught by Greenfield, for, in the **sclerous** form of atheroma, as has been pointed out, **obliterative** changes are not by any means constant. The vessels are frequently dilated. Again, in the true **obliterative,** or, preferably, **proliferative,** form of endarteritis, such as is seen in the healing of wounds, the newly-formed tissue is vascular and really inflammatory in nature; and we therefore think it well to confine the term to conditions which shew these characteristics.

The term arterio-sclerosis Russell confines to those cases in which there is " a marked thickening of the tunica media due to a hypertrophy of its muscle-fibres; a thickening of the tunica intima due to a hyperplasia of its subendothelial connective tissue, without atheromatous degeneration; and, in some instances, fibrous hyperplasia and thickening of the tunica adventitia."

(*i*) **TUBERCULOUS DISEASE** of the arteries needs only to be mentioned. The arteries may become involved in the local spread of a tuberculous focus precisely in the same way as other tissues—the tubercles being mainly found in the adventitia, and, in cases of tuberculous meningitis, these changes are specially well seen in the pial and perforating vessels. The weakening of the wall produced by the caseation may lead to aneurismal dilatation. More rarely, a tuberculous affection of the intima, simulating that seen in syphilis, occurs. In the development of tuberculous lesions, obliteration of the vessels takes place **in** the nodules, though there may be increased vascularity **around** them.

[1] Russell, *Arterial Hypertonus, Sclerosis and Blood-Pressure,* William Green & Sons, Edin. and Lond., 1907.

(*j*) **PERIARTERITIS NODOSA.**[1]—This is a rare condition—a true peri-arteritis—nodular in its distribution. It is probably a manifestation of syphilis and may affect especially the arteries of the brain.

(*k*) **POLYARTERITIS ACUTA NODOSA** is a disease of great rarity, the first case in this country having been described by one of us.[1] It occurs mostly in males, and is characterised by the formation of small localised nodules upon the smaller and medium-sized arteries. These nodules show local inflammatory changes, necrosis of the vessel-wall (especially of the media), usually with the

Fig. 262.—*Acute Nodose Polyarteritis.* Longitudinal section of a small artery from mesentery, shewing break in internal elastic lamina and muscular coat, and formation of minute aneurism. Organising thrombus in lumen. Carnegie Dickson's case. (Unna's modified orcein method for elastic tissue.) × 100.

formation of a small aneurism, and thrombosis of the contents of the lumen and of its aneurismal dilatation. There is, in addition, rupture of the internal elastic lamina and often considerable thickening of the intima. The arteries mostly, attacked are those of the heart and kidneys, and sometimes those of the mesentery, liver, stomach, intestines, muscle, etc.—very rarely those of brain or lungs. In these organs and tissues, secondary changes such as infarction, necrosis, hæmorrhage, etc., may occur from blocking of the arteries. In a case described by Beattie and Douglas,[2] death resulted from rupture of an

[1] Carnegie Dickson, " Polyarteritis Acuta Nodosa and Periarteritis Nodosa," *Jour. Path. and Bact.*, Cambridge and London, 1907, vol. xii. p. 31.

[2] Beattie and Douglas, " A Case of Polyarteritis Acuta Nodosa," *Jour. Path. and Bact.*, Cambridge, 1912, vol. xvii. No. 2, p. 195.

aneurism in the kidney, and there was a deposit of fibrin in, and a leucocytic infiltration of, the adventitia of the affected arteries. The cause of the condition is unknown, though the general histological appearances, in the case described by Beattie and Douglas, suggested a bacterial infection, and the clinical history supported this view. No organisms could be demonstrated in the actual vascular lesions, but a pure growth of streptococci was obtained from the blood round the ruptured aneurism.

(*l*) **RHEUMATIC FEVER AND ARTERIAL LESIONS.**—Thickening of the peripheral arteries has been described as secondary to acute articular rheumatism; and some authors regard rheumatism as an important factor in the production of many of the thickenings seen in later life. Proliferative endarteritis and diffuse mesarteritis have both been described and, as a result of the mesarteritis, the formation of aneurisms has been explained. Some of the cases of polyarteritis acuta nodosa have been associated with attacks of acute rheumatic fever. The evidence seems sufficiently strong to establish the position that acute rheumatism is a factor in the production both of arterio-sclerosis and of aneurism. Klotz [1] has described the production of an acute sac-cular aneurism in a boy of six years, during an attack of acute rheumatism with severe valvular disease, and, in this case, there was a well marked mesarteritis. A streptococcus was grown from the blood and from the spleen. Somewhat similar changes, with necrosis, fibrin-formation and accumulation of leuco-cytes, have been described as occurring in pneumonia, in ulcerative endo-carditis, and in scarlet fever.

ANEURISM

An **aneurism** may be defined as a more or less circumscribed dilatation of a vessel or of the heart-wall. The term, however, is also somewhat loosely used for localised collections of blood, either between or in the layers of the vessel-wall, or even for collections which are surrounded by a more or less well-defined envelope, though they be altogether external to an artery. We propose, here, to confine the term aneurism to the **true** variety—a dilatation of a vessel, and particularly of an artery. Aneurism of the heart has been described on p. 525, and dilatations of veins will be referred to later.

Ætiology.—Aneurisms are due to local weakening of the vessel-wall, and their production is aided by any increased pressure within the vessel. Thus, any process which produces degenerative changes in the vascular system may be regarded as a possible cause of aneurism. The condition is of most frequent occurrence in persons about the age of forty or forty-five, and in those whose vessels shew arterio-sclerotic changes. Among the common primary causes are syphilis (in at least 50 per cent. of cases), alcoholism, gout, lead-poisoning, and other chronic intoxications. Rheumatic fever, and possibly other acute infections, by producing a more or less acute endarteritis, may be important causal agents. These factors are aided by increased blood-pressure, and, for this reason, aneurisms are most frequently found in those who are subjected to severe muscular strain and are, therefore, much commoner in males than in females. The

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[1] Klotz, " Arterial Lesions in Rheumatic Fever," *Jour. Path. and Bact.*, 1913, vol. xviii. No. 2, p. 259.

occurrence of aneurisms in Bright's disease is probably due to the degenerative changes in the wall of the vessel brought about by the chronic toxæmia, but there seems little doubt that the persistent high pressure in the vascular system is an important contributory cause. The degenerative changes and the loss of contractility and elasticity in the media diminish the resistance to the distensile force of the blood; and probably, in the majority, if not in all, of the cases, this degeneration is essential to the production of the dilatation. Destructive changes in the walls of the arteries may also be produced by direct injury : by the spread of ulceration from outside, è. g. aneurism of the splenic artery resulting from the involvement of that vessel in ulceration of the stomach, or aneurism of a branch of the pulmonary artery due to destructive changes in a phthisical cavity : or by sepsis involving the artery from within, as occurs in septic embolism or in the local spread of malignant endocarditis into the aorta.

Sites of Aneurisms.— The artery most commonly affected is the **aorta,** and, in particular, its thoracic portion. The aneurism starts, as a rule, in the region of the sinuses of Valsalva, and, eventually, may involve especially the ascending part of the arch. Sometimes, the aneurisms are multiple, and an aneurism of the thoracic aorta may be associated with one or more on the abdominal aorta. Next in point of frequency to the aorta, the **popliteal, femoral, carotid, subclavian, axillary, innominate, iliac, cerebral,** and various **visceral arteries** are affected.

Fɪɢ. 263.—Aneurism of Abdominal Aorta filled with thrombus. (Edinburgh University Anatomical Museum. Catalogue No., Cir. G. f. 1.)

Though larger aneurisms of the cerebral arteries are comparatively uncommon, minute or **miliary** aneurisms are of not-infrequent occurrence. They affect especially the smaller-sized blood-vessels of the brain— particularly the branches supplying the lenticulo-striate body—and the retinal arteries.

Aneurisms resulting from emboli are most commonly found in young people, especially in the cerebral, though they may also develop in the peripheral, vessels. They are probably due to stretching of the degener- ated, and perhaps necrotic, vessel-wall by the increased pressure behind the obstruction.

Fig. 264.—Section through a laminated Thrombus in an Aneurism of the Aorta.
(Pathological Museum, University, Sheffield.)

Varieties and Structure.—True aneurisms may be divided into two main varieties :—

(1) Those in which there is primarily a general, and more or less uniform, dilatation of all the coats of a vessel—the **fusiform** aneurism. As the dilatation increases, there may be thickening of the inner and outer coats, with atrophy of the media. This atrophy is usually only partial, but, at places, there may be complete disappearance of the muscular tissue. More rarely, the inner coat also undergoes atrophy.

(2) Those which are really pouches from the vessel—a local unilateral dilatation taking place at a weakened part of the vessel-wall. These **saccular** aneurisms usually communicate with the vessel by a more or less narrow opening. The wall of the aneurismal sac, like that of the

fusiform aneurism, may shew evidence of the presence of the three coats of the vessel, with, however, the media usually atrophied and the intima thickened and atheromatous. In other cases, it may be impossible to trace the constituent coats.

Thrombosis is a very common occurrence in this class of aneurism, and the thrombus is deposited in successive layers (*see* figs. 263 and 264). This laminated thrombus may more or less completely fill up the sac, and organisation may take place. If the aneurismal sac is small, complete healing is sometimes brought about by this process of thrombosis and organisation.

Miliary Aneurisms.—These aneurisms are of the sacculated variety, are very small, and may even be microscopic in size. As already stated, they are found especially on the arteries of the brain and of the retina. They are usually multiple and occur on arteries which shew arteriosclerotic changes, and are commonly associated with hypertrophy of the left ventricle. Some of them have been described as dissecting aneurisms, but this is difficult to demonstrate conclusively. **Rupture** of these minute aneurisms is a frequent cause of cerebral hæmorrhage. In this class of aneurisms are included minute bulgings of the middle and inner coat or of the inner coat alone through a degenerated outer coat. Some of the minute aneurisms on the pulmonary vessels in cases of phthisis are of this nature, as are also the miliary aneurisms described by Charcot as due to a sclerous periarteritis. The lesions of polyarteritis nodosa (*q.v.* p. 554) are generally of the nature of minute aneurisms.

In **Dissecting " Aneurisms "** resulting from degenerative changes in, or from mechanical injuries to, the intima, the blood in the artery makes its way between the inner and middle coats or between layers of the middle coat, and burrows, it may be, for considerable distances. By rupture of the wall of the vessel, it may eventually make its way either externally, or back into the lumen. These so-called aneurisms are most commonly found between layers of the middle coat, and may cause atrophy of the muscular tissue. They generally arise through the cracking across of an atheromatous patch, but they also occur as the result of ulceration spreading from the aortic valves and involving the first part of the aorta.

Shennan [1] has described several cases in which, though the pathological changes were in the middle coat, there was no atheroma or other, gross lesion in the intima. The medial changes were fatty degeneration of the connective tissue closely apposed to the elastic lamina, increase of the connective tissue between the laminæ, hyaline degeneration of this connective tissue, thinning or varicosity of the elastic fibres, rupture of these, and sometimes rupture of numerous adjacent fibres. Atrophy with disappearance of the muscle-fibres occurs sometimes over a consider-

[1] Shennan and Harvey Pirie, " The Etiology of Dissecting Aneurism," *Brit. ed. Jour.*, November 9, 1912.

able area in the middle and also in the outer part of the wall. As a result of pressure, the intima is bulged into this degenerated part of the media and may rupture. The plane in which the blood travels is partly determined by the site of the degeneration in the middle coat.

The so-called **False Aneurism** is really a hæmatoma. By traumatism or spontaneous rupture of a vessel, the blood escapes into the surrounding

FIG. 265.—Section through an Aneurism of the descending Aorta, eroding the vertebræ, the bodies of which are more affected than the intervertebral discs which are seen projecting into the cavity of the aneurism. This has been opened into from behind by mesial section through the spine, the two halves of which have been separated from each other.

tissues, where it becomes encapsulated by condensation of these tissues, or by their inflammatory or irritative proliferation.

Sometimes a wound perforates both an artery and a vein, a direct connection may be established, and the vein become markedly distended by the blood which passes in from the artery. Such a condition is known as an **aneurismal varix.** Again, the connection between the two may not be direct, but may take place by an adventitious sac formed by a condensation of the intervening tissues, and to such the

name **varicose aneurism** is applied. A varicose aneurism may also be produced by a saccular aneurism pressing upon, and eventually opening into a vein.

The terms " **Circoid Aneurism** " and " **Anastomotic Aneurism** " are applied to conditions where there is a mass composed of dilated and thickened vessels in the subcutaneous tissues. There is no aneurismal dilatation in these cases, and the term " aneurism " in connection with them is wholly misapplied.

Conditions associated with, and Terminations of, Aneurisms.—The general tendency of aneurisms is to enlarge progressively—the surrounding tissues being pushed aside or absorbed as a result of the pressure. The enlargement is not always in the direction of what appears to be the line of least resistance. Thus, an aneurism of the thoracic or abdominal aorta may enlarge posteriorly and cause erosion of the vertebral bodies, even coming to press on the spinal cord. In this erosion, the inter-vertebral discs do not suffer to such a degree as the vertebræ themselves, and may be seen projecting beyond the surface of the eroded bones (see fig. 265). Enlargement may, however, take place in any direction, and thus important structures may be pressed upon and their function interfered with, or they may even be completely destroyed. An aneurism of the thoracic aorta may press on and erode the sternum; may cause compression of the trachea or bronchi, and thus produce collapse of the lungs; may compress and open into some of the larger veins; or may cause laryngeal paralysis by pressure on the left recurrent laryngeal nerve.

Hypertrophy of the left ventricle is frequently described as occurring in cases of aneurismal dilatation; but, in our experience, it is *not* usual, unless there is some associated narrowing or dilatation of the aortic orifice, or the presence of some independent cause of hypertrophy, e. g. Bright's disease.

Spontaneous cure by thrombosis and organisation is rare. **Rupture** may occur in any situation or into any adjoining cavity, organ, or tissue. Aneurisms of the thoracic aorta may burst into the pericardial or pleural sacs, into the trachea or bronchi, into the œsophagus, the vena cava, the mediastinum, or, much more rarely, externally, after the skin has become stretched and eroded.

(C) DISEASES OF VEINS

DILATATION AND VARICOSITY.—The veins possess a great capacity for dilatation, and, therefore, any mechanical obstruction to the circulation or any weakness of the walls of the veins may give rise to very great enlargement. The obstruction in one vein leads to obstruction and dis-tension of its tributaries. Accompanying the dilatation, if not merely transitory, there is also elongation of the vessels, which, in consequence, thrown into folds and become varicose.

Causation.—Mechanical causes are, perhaps, the most important. Thus, if there is obstruction to the portal circulation by tumours, by cirrhosis of the liver, or by other causes, great distension and varicosity of the veins of the rectum and of those at the lower end of the œsophagus may occur. Pressure, due to tumours, repeated pregnancies, etc., upon the veins returning blood from the lower limbs, may give rise to varicosity of the veins of the lower limbs. These causes are in themselves sufficient to produce this condition; but they are, no doubt, aided by weakening of the walls of the vessels, absence or diminution of the external support of the surrounding tissues, and cardiac conditions in which the circulation is greatly impeded. Gravity plays some part in the process, as is evidenced by the frequent occurrence of varicose veins in the legs of those whose occupation demands a great amount of standing.

Pathological Anatomy.—The dilatation and varicosity of the veins are accompanied by thickening of their walls, and usually by incompetence of the valves—this incompetence increasing the dilatation and the varicosity. The thickening of the walls of the veins is especially marked in the inner coat, which sometimes becomes calcified. Degenerative changes take place in the muscular coat, and calcification may also occur in it. The outer coat may shew proliferative changes. Thrombosis is very liable to occur in the dilated veins. Such thrombi may undergo organisation, or they may become calcified, forming **phleboliths** or "**vein-stones**"; or they may become detached, in whole or in part, and give rise to **embolism.** The separation of the thrombi, with the formation of emboli, is more likely to occur in cases in which septic infection, with consequent softening, takes place. The tissue round

FIG. 266.—Thrombosis in the Iliac and Femoral Veins. Adhesion and partial organisation of the thrombus towards the upper part. (Edinburgh University Anatomical Museum. Catalogue No., Cir. H. a. 3.)

the diseased veins may shew chronic inflammatory changes. Thus are to be explained the chronic eczematous condition of the skin and the

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thickening of the subcutaneous tissue so frequently associated with varicose veins. On the other hand, the pressure of the dilated vessels often causes atrophy of the surrounding parts. Ulceration of the superjacent skin and other tissues may occur, and ulcers so produced are usually very indolent and persist for years. The vein may rupture or may be opened into by the ulceration, and thus serious hæmorrhage be produced. This hæmorrhage, by rupture, is perhaps commonest from the varicose veins—**hæmorrhoids**—of the lower parts of the rectum : or from those at the lower end of the œsophagus in cases of cirrhosis of the liver.

Situations in which varicose veins most commonly occur :—

1. **The veins of the lower limbs.**

2. **The veins of the lower part of the rectum,** immediately under the mucous membrane. These veins communicate with the inferior mesenteric vein—a tributary of the portal vein—and with the internal iliac— a tributary of the vena cava. Thus, any obstruction to the portal circulation or any abnormal pressure in the intestines or in the abdominal cavity may cause dilatation of the venous plexus. The veins become varicose, and bluish knots, varying in size, are seen pushing the mucous membrane before them. These **hæmorrhoids** or **piles** may rupture ; thrombus formation may take place in them ; and chronic inflammatory changes may occur around them.

3. **The veins of the spermatic cord.**—Dilatation and varicosity of these—**varicocele**—occur especially on the left side, due no doubt to the circuitous course of the left spermatic vein. It has been stated that this condition causes **atrophy of the testicle,** and that it may give rise to **hydrocele** or **hæmatocele.**

4. **The veins of the neck of the bladder and prostate** in the male, and **of the vagina and broad ligament** in the female ; and those **of the dura mater** and **of the lower end of the œsophagus,** may be the seat of **varices.**

INFLAMMATION.—This condition frequently occurs in veins which are dilated and varicose. It may spread from neighbouring inflammations, resulting from infected wounds, erysipelas, etc., as in the thrombosis of the lateral sinus, secondary to suppurative middle ear disease. **Microscopically,** in such acute cases as arise by spread from neighbouring inflammatory areas, there is found an invasion of the various coats of the vein by inflammatory cells. Thrombosis frequently occurs, and the thrombi thus formed may become infected, and may soften, break down, and form emboli. In a second group of cases, the inflammation starts from within, and is most commonly the result of septic infection. Septic matter is introduced into the vein and induces thrombosis. This septic thrombus, however produced, acts as an irritant to the inner coat of the vessel, and causes an exudation of leucocytes, which infiltrate the various coats of the vessel—the thrombus eventually breaking

down, and the vessel becoming filled with a purulent material. This septic exudate, which is distributed by the blood-stream and becomes lodged in various situations, causes multiple abscess-formation, and is liable to produce all the phenomena of **pyæmia.** Non-septic phlebitis is said to occur. It is always associated with thrombosis, and has been called "**thrombo-phlebitis.**" It may arise as a result of injury to the vessel-wall. The thrombus formed undergoes organisation, in whole or in part, and may become calcified, or be partially absorbed, leaving a thickening of the wall of the vein, especially of its inner coat. There may, however, be, in addition, some proliferation of the connective-tissue cells of the media. A similar condition which has been called "**phlebo-sclerosis**" is said to occur in cases of syphilis and gout.

THROMBOSIS IN VEINS is fully dealt with on p. 142.

DEGENERATIONS.—Fatty and **Waxy** or **Amyloid** degenerations are not uncommon, but the changes in the veins due to these conditions have been described in Chapter II.

Reference has already been made to **Calcification.**

GRANULOMATA.—Tuberculous disease in any organ may spread so as to involve the veins, and, by destruction of their walls, the tuberculous material reaches, and is distributed by, the blood-stream, giving rise to a general tuberculosis.

Syphilis produces, as a rule, much less evident results in veins than in arteries. Definitely marked histological changes in the veins are uncommon, but gummatous infiltration and syphilitic endo-phlebitis are described, as is also the condition of syphilitic peri-phlebitis, which is occasionally nodose in its distribution.

TUMOURS.—Tumours of various kinds involve secondarily the walls of the veins, and may spread along their lumen. Of primary tumours, **myomata** and **sarcomata** have been described, but they are rare.

DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS

INTRODUCTORY.—Before passing to the systematic description of the diseases of the blood and blood-forming tissues, it may be well to give a short *résumé* of the **composition of the blood in health,** and also of our present knowledge with regard to the **origin and development of the formed elements** in the **hæmopoietic** or **blood-forming tissues,** such as the **bone-marrow** and the **lymphatic glands.** In the past, attention has been devoted chiefly to the morphological characters of the formed elements of the blood —the different varieties of **leucocytes,** normal and abnormal, their total and their relative numbers, and the degenerative and other changes occurring in them : the number, size, shape, and contents of the **red corpuscles:** the number of **blood-platelets** present, and similar phenomena. Recently, much work has been done in connection with the **physics** and **chemistry** of the blood, and also with regard to its **bacteriology** and **parasitology.** The most remarkable recent advances have been the discovery of certain apparently **specific substances** which are either **normally present** in the blood, or are **developed in it as the result of disease**— natural or experimental—and which are known as hæmolysins, agglutinins, precipitins, coagulins, opsonins, bacteriolysins, etc. The chemistry and nature of these bodies are still but little understood, and their presence can be determined only by certain delicate bio-chemical and other tests which are as yet more or less empirical in their results. A more detailed account of some of these substances and their reactions will be found in the chapter on **Immunity** (p. 450).

    THE TOTAL VOLUME OF THE CIRCULATING BLOOD.—The older estimate that, in man, the total amount of blood was about one-thirteenth of the body weight, has, by more recent scientific methods, been found to be somewhat excessive. Haldane and Lorrain Smith estimate the average amount to be 4·78 per cent., or about a **twentieth** (with a variation of from about a thirtieth to a sixteenth). If the total fluid bulk of the blood is artificially increased or diminished, rapid readjustment as regards volume takes place.

DESCRIPTION OF PLATE XIV

PLATE XIV

Fig. 1.—*Film of Normal Blood* (stained with hæmatin and eosin). ▓▓▓ Red blood-corpuscles are regular in outline and in size.
 a.a.—Polymorphonuclear leucocytes.
 b.—Eosinophil leucocyte.
 c.—Small lymphocyte.
 d.—Large hyaline leucocyte.
 e.—Blood-platelets.   ×500

Fig. 2.—*Blood-Film from a case of Neutrophil Polymorphonuclear Leucocytosis* (stained with eosin and methylene-blue).
 a.a.—Polymorphonuclear leucocytes.
 b.—Medium-sized lymphocyte.
  The red corpuscles do not exhibit any obvious changes.   ×500

Fig. 3.—*Blood-Film from a case of Myelocythæmia* (stained with Jenner's stain).
 a.a.—Adult polymorphonuclear neutrophil leucocytes.
 b.b.—Immature polymorphonuclear neutrophil leucocytes.
 c.c.—Intermediate neutrophil myelocytes.
 d.d.—Small neutrophil myelocytes.
 e.e.—Large neutrophil myelocytes.
 f.—Non-granular mononuclear cell, possibly a pre-myelocyte or parent-cell of the granular myelocyte.
 g.g.—Eosinophil myelocytes.
 h.h.—Mast-cells.
 i.—Small lymphocyte.
 k.—Large lymphocyte.
 l.l.—Normoblasts.   ×500

Fig. 4.—*Blood-Film from a case of Lymphocythæmia* (stained with Leis'.man's stain).
 a.—Polymorphonuclear leucocyte.
 b.b.—Small . . . ⎫
 b′.b′.—Medium-sized ⎬ Lymphocyte-like cells.
 b″.b″.—Large . . . ⎭
 c.—Normoblast.
 c′.—Normoblast with fragmented nucleus.   ×500

Plate XIV. Vol. II.
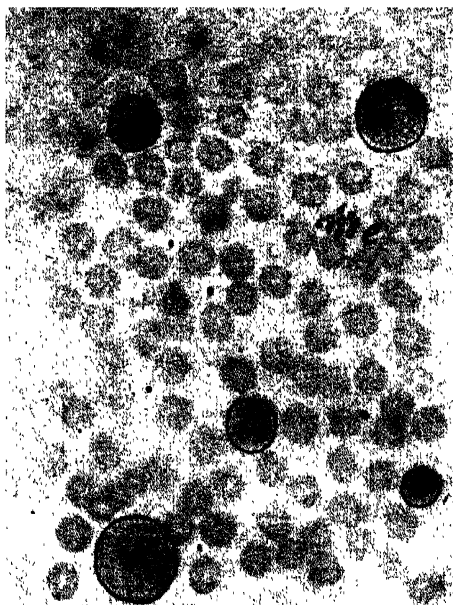
Fig. 1.   Fig. 2.
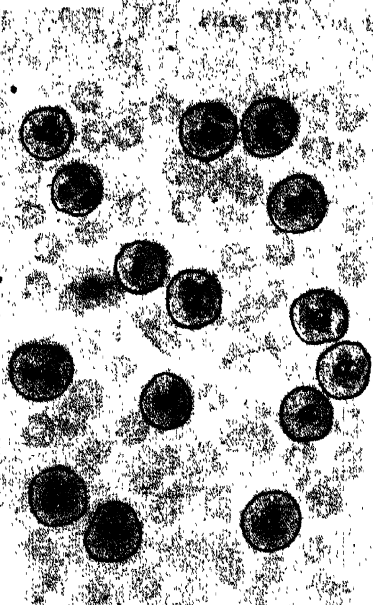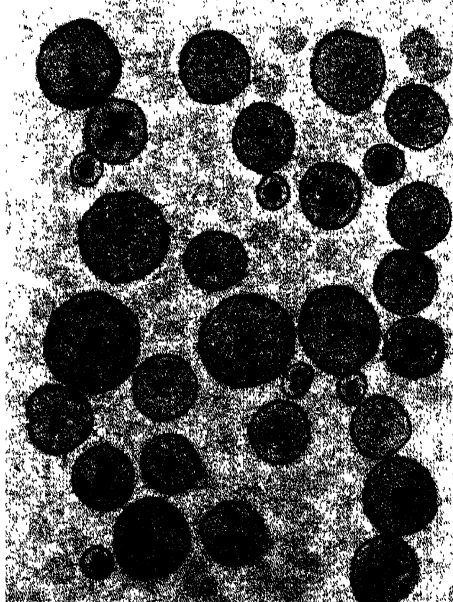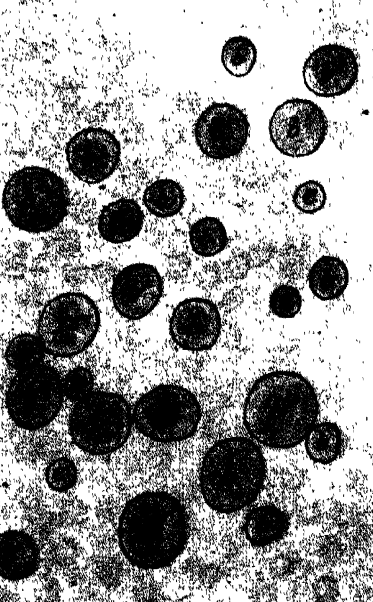
I. CONDITIONS OF THE PLASMA AND OF THE BLOOD AS A WHOLE

The **CHEMISTRY** of the blood is extremely complex, and little is yet known of the ultimate nature of many of its constituents. In the **blood-plasma, liquor sanguinis,** or **fluid portion** of the blood, are dissolved or suspended—in addition to innumerable other substances—the **nutrient material** which it conveys to the tissues, and the various **waste-products** which arise during metabolism, and which are carried to certain organs to be destroyed or excreted. Similarly, the "**internal secretions**" elaborated by various organs and tissues are distributed by the blood and lymph, through the agency of which they act upon the various structures of the body.

The blood is thus constantly changing in its composition. The **relative amount of fluid** and the **absolute and relative numbers of the formed elements** vary considerably, not only in different individuals, but also from time to time in the same individual and in different organs and tissues of the body.

Thus, in the interpretation of observations upon the blood, many considerations have to be borne in mind. These are well summarised by Ewing [1]—who also adds that : "the examination having been performed, **its results are to be interpreted only in the light of the fullest possible clinical information**"—as follows :—

" 1. There are considerable physiological variations in the volume and composition of the blood, according to the constitution of the individual (plethora), and the degree of muscular development. Here may be classed the variation between the sexes and between the different periods of life. Such variations are permanent, but usually not of extreme grade.

" 2. There is a great variety of physiological conditions producing marked but transitory changes in the blood, such as active digestion, muscular exertion, the ingestion of fluids, profuse perspiration, temporary cyanosis, etc.

" 3. The nervous system has a very striking temporary influence on the quality of the blood in local or general areas, acting through the cerebral (psychical) or medullary centres, or through local vasomotor nerves.

" 4. Various local influences may greatly change the quality of the blood-specimen, as seen in the local and transient effects of cold, heat, massage, and electricity.

" 5. Many therapeutical procedures may temporarily alter the blood, as the aspiration of fluids, administration of diaphoretics, purges, vasodilators (amyl nitrite), vasoconstrictors, etc.

" 6. Various pathological conditions may partly or completely obscure the real status of the blood, as the sweats of phthisis; the diarrhœa of typhoid fever, dysentery, and cholera; general cyanosis or local stasis; the increased arterial tension of uremia; the polyuria of diabetes and nephritis; *ante-mortem* cardiac failure, etc."

The blood contains from rather more than one-third to one-half its

[1] Ewing, *Clinical Pathology of the Blood,* 2nd edition, Kimpton, London, 1904, p. 20.

weight of corpuscles, and from 20 to 25 per cent. solids. The **Blood-plasma** is resolved, on coagulation, into **Serum** and **Fibrin,** the latter forming only from 0·2 to 0·4 per cent. of the total weight of the blood. The serum contains 8 to 9 per cent. solids, of which 7 to 8 per cent. consist of proteins and about 1 per cent. of salts. The **protein-content of the serum** consists chiefly of the two series of coagulable proteins, the **serum-albumins** and the **serum-globulins,** the total amount of which, as a rule, remains more or less constant, and is about 8 per cent. by weight of normal serum. The ratio of these substances to one another, however, varies considerably both in health and in disease, but further observations are required before any definite rule can be laid down with regard to these variations. This ratio is known as the " **protein-quotient.**" It varies in different animals, but, in the same animal, it is almost constant in the blood, serum, lymph, and serous transudates, though the total protein-content of these fluids may be very different.[1] The globulin-fraction of the serum-proteins is again divisible into two farther fractions : **euglobulin,** which can be precipitated by dialysis : and **pseudoglobulin,** which is not so precipitable, but is thrown down on half-saturation with ammonium sulphate. Serum-globulin molecules are of large size and will not pass through a porcelain filter: They are probably of importance in relation to various " **adsorption** " **phenomena** discussed in the chapter on **Immunity** (p. 450). The albumin-content of the serum is said to be considerably diminished in severe anæmias and in cases of dropsy.

Traces of numerous **nitrogen-containing substances** such as **urea, uric acid,** etc., are present in the blood and may be slightly increased in acute fevers, uræmia, leucocythæmia, etc.

Glucose in very small quantity is normally present, and has been found to be increased in cases of diabetes, in which its amount varies greatly. **Hyperglycæmia** (to the extent of 0·4 to 0·5 per cent.) and glycosuria follow the **experimental excision of the pancreas** in animals—whether the animals are starved or fed upon a protein or protein-and-fat diet—owing to loss of the secretion of the islets of Langerhans.

Glycogen in the plasma and in the leucocytes may be demonstrated microscopically by its brown staining-reaction with iodine. In finely granular form, it is normally present in the plasma; whilst it is also found, sometimes in large amount, in the leucocytes, particularly the **neutrophil polymorphonuclears (glycogenic reaction** or **iodophilia),** in certain pathological conditions, notably in cases of fever, leucocythæmia, and in certain toxæmic conditions, especially in septicæmias, and in acute inflammatory and suppurative diseases. In tuberculosis; the glycogenic reaction of the leucocytes is said to occur only if there are suppurative complications; and in diabetes, only if coma, suppuration, or gangrene

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[1] Most of the information in this paragraph is taken from Starling's *Principles of Human Physiology,* 2nd edition, Churchill, London, 1915, which should be consulted for details.

supervene—though, in diabetes itself, the *extracellular* glycogen in the blood-plasma is usually increased.[1]

Fatty Substances.—These vary considerably in amount in different individuals, and also with the quantity of fat ingested and absorbed. **Lipæmia,** or abnormal increase of fat in the blood, may occur in certain cases of diabetes. Such blood, when freshly drawn, shews a milky pinkish colour, and, on standing, separates into various strata, the supernatant fatty layer often being of very considerable thickness. In certain cases in which the oxidative capacity of the body for fats is inadequate, as the result either of disease or overstrain of the fat-oxidising powers, *e. g.* in the **acute acidosis** in the terminal stages of diabetes, **acetonuria** occurs. The acetone, and the β-**oxybutyric** and **diacetic acids** also occurring in the urine in such cases, were formerly thought to be derived from the carbohydrates of the food or from sugar abnormally produced in the body. In many cases, however, the acidosis is induced by the carbohydrate-starvation employed in the treatment of such patients, and these acids are derived from the fats, and perhaps also from the proteins, of the body and food. A similar result is obtained on giving an exclusively or excessively fatty diet in health. The partially oxidised fatty acids, β-oxybutyric and diacetic acids, accumulate in large quantities in the blood and are excreted in the urine, chiefly as acetone, though the acids themselves may also be found. " **Acetonæmia,**" or, perhaps more accurately, **acidosis,** and **acetonuria** may be present, particularly in children, in delayed chloroform-poisoning, in some cases of peritonitis, and in certain febrile attacks of unknown origin—sometimes occurring as epidemics—which may be recurrent in the individual cases affected.

Bile-acids, bile-pigment, and also, it is said, **cholesterol,** are present in considerable amounts in **cholæmia** or **jaundice.**

Various inorganic salts, such as phosphates, chlorides, carbonates, and sulphates, are normally present in the blood-serum. Of these, **sodium phosphate** and **chloride** are present in greatest amount. Variations in these do not appear to be very marked in disease.

PHYSICAL CHARACTERS OF THE SERUM.—The pale-yellow or slightly greenish-yellow tinge of the serum is due to the presence of certain **fatty pigments** or **lipochromes.** In acute toxic diseases characterised by marked blood-destruction, the blood-serum may present a reddish tint, due to the presence of hæmoglobin extravasated from the injured red corpuscles. This is, however, as a rule, only slight in amount, and, in such toxic conditions, the colour is more usually orange-red from the presence of bilirubin.

The specific gravity of the serum varies, in a state of health, from 1·025 to 1·030; **that of the blood as a whole** from 1·050 to 1·060.[2] The variations

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[1] For further details of this reaction, see W. Herbert Brown, " A Clinical Study of the Glycogenic Reaction in Blood," *Practitioner,* January 1910, p. 87.

[2] Lloyd Jones states that, in childhood, the specific gravity of the whole blood is 1·050, gradually increasing until, at seventeen, it is 1·058 in the male and 1·0556

are due to changes in the proportional amount of fluid, and also, but to a less extent, in the relative amount of solids, more especially of salts, present. It is, naturally, lower after the absorption of much liquid into the blood, and higher after sweating, diarrhœa, etc. In anæmias, the specific gravity of the blood as a whole is lowered, usually in direct proportion to the diminution in the amount of hæmoglobin.

Osmotic tension.—When the osmotic tension of the salts in the plasma is normal, the hæmoglobin in the red corpuscles is retained within them; but, if this relationship is sufficiently altered by the addition of water, the corpuscles become "laked," i. e. the hæmoglobin passes out into the plasma. In terms of the strength of a solution of common salt, the osmotic tension of the blood-plasma is about 0·9 per cent.

Alkalinity.—The relative degree of alkalinity of the blood is due to the presence of carbonates and other salts. No very constant results have, as yet, been obtained in the estimation of the alkalinity of the blood, that of the plasma, and that of laked blood—i. e. the whole blood in which the contents of the corpuscles have been freed—differing considerably from one another. The method devised by Wright is the one now most commonly adopted for estimating the alkalinity, but it still remains to be seen whether the results of such observations are of much clinical value.

Coagulability.—The investigation of the coagulability of the blood is a point of considerable importance in connection with the various " **bleeding** " **diseases,** such as scurvy, purpura hæmorrhagica, the so-called hæmorrhagic diathesis, etc. In these conditions, coagulation may be indefinitely **delayed;** and it may also be delayed in the acute infective fevers, in some of the anæmias, and in cases of jaundice. The coagulability may be estimated by the length of time taken for drawn blood to coagulate in a series of capillary pipettes (Wright's method), or by breaking across, at definite time-intervals, a capillary tube of sufficient length filled with blood, and observing the time taken for a clot to form, as suggested by M'Gowan. Addis[1] is of opinion that the cause of the delay in the coagulation of hæmophilic blood is a qualitative defect in the prothrombin (see p. 627). The coagulability of the blood tends to be **increased** in pneumococcal infections, intracardiac thrombosis being an important complication, especially in acute lobar pneumonia. An increased liability to thrombosis is also described in chlorotic anæmias. The general subject of **Thrombosis** is discussed in Chapter V, p. 137.

The Freezing-point of the Blood has been investigated, more especially in connection with its relationship to that of the urine, in diseases of the

in the female. Thereafter it continues to increase in the male; whereas in the female it may diminish again during the establishment of menstruation, but increases again after twenty-five, at which age it is 1·055 or 1·056. There is, therefore, normally a fall in the female after puberty, a fact of importance in the consideration of the age-incidence of chlorosis (see p. 617).

[1] Addis, " The Pathogenesis of Hereditary Hæmophilia," Jour. Path. and Bact., vol. xv., No. 4, 1911, p. 427.

kidneys, the freezing-point being lowered by the presence óf greater quantities of dissolved salts; etc., and *vice versa.* The process of testing the freezing-point is known as " Cryosoopy."

Various **Ferments,** oxidising, fat-splitting, glycolytic, etc., are described as occurring in the blood.

A subject upon which a considerable amount of work has recently been done, especially in America, is the existence of several—probably four— **" types "** of•human blood, a knowledge of which is of great importance to surgeons and others who may be called upon to perform the operation of transfusion of human blood for the treatment of cases of hæmorrhage, pernicious anæmia, hæmophilia, septicæmia, etc. Quite apart from the risk of transmitting such diseases as syphilis, malaria, etc., it has been found by experience that serious, and sometimes even fatal, results may follow the intravenous injection of an **" incompatible "** blood—vomiting, dyspnœa, urticarial skin-eruptions, rapid feeble pulse, and, perhaps, convulsions or coma, and even, in some cases, death, supervening. In order to minimise these risks, tests should always be carried out to ascertain whether the donor's blood will not (*a*) agglutinate, and (*b*) hæmolyse the red corpuscles of the patient—the two phenomena usually running parallel with one another.

Moss [1] states•that there are probably four such types, the suitability of which for transfusion he gives as follows :—

DONOR.	PERCENTAGE FREQUENCY.	SUITABLE IF PATIENT belongs to :—
Group I	5	Group I.
„ II	40	„ I, II.
„ III	10	„ I, III.
„ IV	45	„ I, II, III, or IV.

For determining these reactions, Vincent [2] has described a simple agglutination-test, for the details of which the reader is referred to his original paper, or to a valuable review of the subject by Rendle Short.[3]

The Presence of Bacteria in the Blood, *e. g.* in typhoid and para-typhoid fevers, streptococcal, and other septicæmias, pneumonia, etc., can best be demonstrated by methods of culture. Sufficient blood—usually 5 or 10 cubic centimetres or more—is withdrawn from a vein, added to some suitable culture-medium in sufficient dilution, incubated, sub-cultured if necessary, and examined.

The Presence of Animal Parasites, *e. g.* protozoa, worms, etc., is dealt with in the Chapter on **Parasites,** p. 346. (*See under* Malaria, Trypanosomes, Filaria, etc.)

Foreign material of extraneous origin is often found when examining blood under the microscope. Particles of dirt, squamous epithelial cells, bacteria and other organisms from the skin, etc., must therefore be carefully differentiated from true pathological material present in the circulating blood.

[1] Moss, *Med. Bull.,* May, 1918, p. 516.
[2] Vincent, *Jour. Amer. Med. Assoc.,* 1918, i, p. 1219.
[3] Rendle Short, " Blood Transfusion," *Med. Annual,* Wright & Sons, Bristol, 1919.

II. VARIATIONS IN THE FORMED CONSTITUENTS OF THE BLOOD, i. e. the Red Blood-Corpuscles, Leucocytes, and Blood-Platelets.

A. ERYTHROCYTES OR RED BLOOD-CORPUSCLES

These are minute, circular, bi-concave, disc-like bodies, which contain the hæmoglobin or red colouring matter of the blood. In the fresh state, they are extremely elastic, and are capable of rapidly returning to their normal shape, even after great distortion. Except in fœtal life and just immediately after birth, they are, in health, devoid of nuclei when they enter the circulating blood from the bone-marrow, where alone, during extra-uterine life, they are formed. They measure about 7·5 to 8·5 μ in diameter. In the adult healthy male, they number about five-and-a-half to six millions per cubic millimetre, and about half a million less per c.mm. in the female. This number is increased in plethora, erythræmia or polycythæmia rubra, and diminished in anæmia or oligocythæmia rubra. In estimating the value of observations upon the number of red corpuscles present, possible temporary variations in the amount of the fluid constituents of the blood must be borne in mind. The hæmoglobin-content may be estimated as so much per cent. of that in health in the blood as a whole, or as so much per corpuscle—in the latter case, the normal colour- or hæmoglobin-index being taken as unity.

Formation of Rouleaux.—In normal blood, after it is shed, the disc-like red corpuscles tend to run together, and adhere to one another by their flat surfaces, forming rouleaux. In some pathological conditions, e. g. the anæmias, this tendency may be only slight, or even entirely absent.

Variations in the Size (Anisocytosis) of the erythrocytes may occur in disease, abnormally large corpuscles being known as megalocytes, those which are diminished in size being termed microcytes, and those of normal dimensions, normocytes. Red cells of corresponding dimensions which still retain their nuclei are known respectively as megaloblasts, microblasts, and normoblasts. Certain red corpuscles of exceptionally large size, and found especially in pernicious anæmia, are known as gigantocytes, or, if still nucleated, as gigantoblasts.

Normoblasts, or nucleated red corpuscles of normal size, are found physiologically in the formative or red bone-marrow. From this, under ordinary circumstances, they should pass into the general circulation only after their nuclei have disappeared; but, in certain conditions in which the equipoise of the hæmopoietic functions of the marrow is disturbed, e. g. after hæmorrhage, in the anæmias and the leucocythæmias, nucleated red cells may pass out into the blood. This may also occur, though usually only to a very slight degree, as an accompaniment of leucocytosis, especially if the latter is very excessive in degree. The passage of erythroblasts into the circulating blood takes place much more readily in children. In some cases of anæmia, the nucleated red blood-corpuscles may become specially numerous just before death; and, in several of such cases observed by the authors, this phenomenon appears

to have been increased by the administration of large saline transfusions —perhaps by the mechanical washing-out of these cells from the bone-marrow.

Megaloblasts, or large nucleated red cells of primitive type, are normally found in the circulating blood during intra-uterine life and for a few days succeeding birth. After this period, they are to be regarded as pathological if found in the circulation. They may make their appearance in such conditions as the more profound anæmias, especially those of pernicious type, e. g. in " primary " pernicious anæmia, and in the anæmias produced by certain intestinal parasites, e. g. *Dibrothriocephalus latus* and *Ankylostoma duodenale.* Except where such parasites are found, the presence of more than a very few of these cells—especially if also accompanied by gigantoblasts and gigantocytes—is sufficient to justify the diagnosis of pernicious anæmia. It may be noted here that, though megaloblasts are rarely found in the blood except in the above conditions, they are by no means of uncommon occurrence in the bone-marrow itself in many diseases, not only in children—in whom they are comparatively common—but also in adults. One of the authors has repeatedly found them in the bone-marrow in such conditions as acute septic diseases, typhoid fever, malignant disease, exophthalmic goître, etc., in the adult; and in diphtheria and many other acute and chronic diseases in children.[1]

Degenerative Phenomena are of common occurrence in red cells (*see* Plates XIII and XVI). The more important of these changes may be summarised as follows :—

Poikilocytosis.—In some diseases, for example in the anæmias, more especially those which are " pernicious " in type, but also in severe secondary anæmia, the red corpuscles may be distorted in shape, and are then known as **poikilocytes** (Plate XVI, figs. 1 and 4). Crenation, or the artificial production of knob-like projections on their surface, due to changes in osmotic pressure, must, of course, be distinguished from this condition.

Fragmentation, or breaking-up of the red cells, is not uncommon, both in the acute toxic diseases and in the anæmias. It is specially common in association with the above described condition of poikilocytosis; and is most frequently seen in pernicious anæmias, this being probably the commonest mode of origin of many of the so-called " microcytes." Some of these abnormally small red corpuscles are, however, undoubtedly derived from parent microblasts, i. e. nucleated forms of small size, by the disappearance of the nuclei of these cells (Plate XVI, fig. 1).

Fragmentation-changes also occur in the **nuclei of Erythroblasts** as these develop into fully formed red cells.

Colour-changes in red cells.—These alterations are most commonly of the nature either of increase, or, more usually, of diminution, in the amount of the contained hæmoglobin. When viewed flat, the normal

[1] Carnegie Dickson, *The Bone-Marrow,* Longmans, Green & Co., London, 1908, pp. 121–122.

red blood-corpuscle, owing to its biconcave shape, is seen to have a paler central part, which represents the correspondingly thinner layer of hæmoglobin in this area. When the hæmoglobin contained within the erythrocytes is diminished from any cause, e. g. in chlorosis and other anæmias, this central pale area becomes exaggerated. In severe cases, it may be perfectly-colourless and transparent, and the hæmoglobin may appear as a more or less scanty pale-red ring around it at the periphery of the cell (see Plate XVI, fig. 2).

In pernicious anæmia, on the other hand, although the total amount of the hæmoglobin in the blood may be markedly reduced, yet the amount per individual corpuscle may shew little or no decrease; or it may be actually increased in quantity, i. e. the colour-index may be above unity, and in this connection it must be borne in mind that, though greatly diminished in numbers, many of the corpuscles may be individually of larger size than normal. In such cases, the corpuscles are darker than normal. Crack-like markings are common in the erythrocytes in severe anæmias, and, though this appearance may in some cases be an artefact, there is no doubt that it does also occur in vivo.

Polychromatophilia or Diffuse Basophilia.—In some conditions, red corpuscles, when stained with methylene-blue and eosin, or some such combination of stains, do not shew the usual bright-red coloration of their discs with the acid stain; but, on the contrary, exhibit a varying admixture of blue staining (Plate XVI, fig. 1). This may occur in two entirely different sets of conditions.

 i. **As a degenerative, and probably necrotic, phenomenon,** supervening in adult or fully-developed erythrocytes as a result of the action of various toxic substances.

 ii. **As a sign of immaturity,** the red cells being rapidly and imperfectly formed in the bone-marrow, and finding their way into the general circulation before they have developed their proper complement of hæmoglobin. That this polychromatophilia is a sign of immaturity is proved by the fact that, in cases in which normoblasts find their way into the blood, these cells, both in the circulating blood and in the bone-marrow, frequently exhibit the condition; and further, the more immature the cells of this series are, the more marked is the degree of polychromatophilia observable in them. The condition is found especially in anæmias, and is usually most pronounced in children.

Punctate Basophilia or Granular Degeneration.—In certain conditions, e. g. in malaria, in pernicious and allied anæmias, and in severe secondary anæmias such as those produced by chronic lead-poisoning, etc., the corpuscles may shew the presence of numerous minute blue-staining points (Plate XVI, fig. 1). The exact origin of these has not yet been ascertained, some regarding them as the remains of the fragmented nucleus, whilst others believe them to be due to degenerative changes in the cyto-

reticulum, and a few hæmatologists even regard them as artefacts. Somewhat analogous points or dots (Schüffner's and Maurer's dots) are of frequent occurrence in the invaded corpuscles in malaria, especially the benign tertian form of the disease. These, however, stain bright red; whereas, often in the same films, the blue-stained points of the punctate basophilia, may be seen in some of the degenerated, but uninfected, corpuscles.

Colour-changes in the Red Corpuscles may also be due to the action of certain poisons of known or unknown nature. Carbon monoxide and sulphuretted hydrogen form compounds with the hæmoglobin. Poisons absorbed from the alimentary canal may similarly form methæmoglobin and sulph-hæmoglobin, and may give rise to a peculiar tinting of the skin and mucous membranes known as enterogenous cyanosis. In some cases, the altered pigment may be retained within the red corpuscles, the change in colour being then mainly due to the inability of the new compound to take up sufficient oxygen. In other cases, if hæmolysis or destruction of the red corpuscles also supervenes, the pigment may be freed into the plasma and be excreted in the urine, meth- or sulph-hæmoglobinæmia and -hæmoglobinuria respectively occurring.

B. WHITE BLOOD-CORPUSCLES OR LEUCOCYTES

In fresh unstained preparations, the white corpuscles appear as clear, colourless, refractile cells, the smaller varieties of which are 7 or 8 μ in diameter, i. e. about the size of the red blood-corpuscles, whilst the diameter of the larger types may be half as large again as, or twice that of, the erythrocytes, or more. If examined under suitable conditions on the warm stage, the polymorphonuclear and large mononuclear cells are seen to be actively amœboid, whilst the smaller lymphocytes are only very feebly so, or non-motile. The fine granules of the polymorph cells, and the coarser granules of the eosinophils, are distinctly visible as highly refractile particles in the protoplasm, with, especially in the latter variety of cell, a pale-greenish tinge due to refraction. "Vacuoles," or clear rounded spaces filled with fluid, are often visible in the cytoplasm, particularly if the cells have been ingesting foreign particles. In the case of the large mononuclear cells, the cytoplasm has a delicately reticulated appearance. When observed on the warm stage, fine streaming, and also to-and-fro dancing, movements, may be observed in the cytoplasm of the polymorphonuclear and large mononuclear leucocytes, especially when these cells are exhibiting phagocytic activities, as, for example, in the freshly-drawn blood of a patient with malaria. In such a specimen, all stages of the phagocytic process may be watched under the microscope, a single large mononuclear cell often being seen to ingest several malarial parasites in succession. Other rhythmic movements may also be noted, for example, a species of pulsatile motion in the walls of the vacuoles, if these be present. It will also be observed that the nucleus of such a cell, or of a polymorphonuclear

leucocyte, during the activities of these cells, does not remain motionless and stationary; but may, from time to time, be seen actively to change its shape and relative position within the cytoplasm.

Diapedesis of leucocytes through the vessel-wall, and their active migration through the tissues, may be observed in suitably arranged specimens, *e. g.* in fresh, moist preparations of frog's mesentery. The polymorph cells are usually the first to leave the vessels, the large mononuclear leucocytes passing out later. In this connection it may be definitely stated that, especially in certain forms of inflammation, the smaller mononuclear cells or small lymphocytes are also amœboid, and can take part in the process of emigration, though much less actively than the foregoing varieties. These phenomena are fully described in the Chapter on **Inflammation** (*see* p. 179).

The presence of **Glycogen** in the cytoplasm of neutrophil polymorphonuclear leucocytes in certain pathological conditions, especially those characterised by neutrophil leucocytosis, is described on p. 568.

VARIETIES AND RELATIVE NUMBERS OF THE WHITE CELLS

In a cubic millimetre of blood drawn from the peripheral circulation,[1] under normal circumstances, there are present about **8,000 white cells.** Variations occur in this number both in health and in disease—a subject to which special reference will be made in the section on **Leucocytosis** (p. 598).

In the following table are enumerated the **varieties** of leucocytes found in the peripheral blood of normal individuals, together with their average **relative** or **percentage** numbers and their **absolute** numbers per c.mm., calculated from 8,000 as the average total leucocytes per c.mm :—

	VARIETY OF LEUCOCYTE.	RELATIVE NUMBERS per cent.	ABSOLUTE NUMBERS per c.mm. (taking 8,000 as Average Total).
i.	Finely-Granular Neutrophil POLYMORPHONUCLEAR Leucocytes . .	60 to 75	4,800 to 6,000
ii.	Coarsely-Granular EOSINOPHIL Leucocytes	1 to 2$\frac{1}{2}$, 3, or even 4 *	80, 200, 240, or 320
iii.	LYMPHOCYTES (Large and Small) .	25 to 45	2,000 to 3,600
iv.	Large Mononuclear HYALINE Cells .	1 to 3	80 to 240
v.	MAST-CELLS	under $\frac{1}{2}$	under 40

* With regard to the number of Eosinophils, *see* p. 577.

It will be clear from the above figures that, in considering the meaning of pathological variations in a **Relative Percentage Leucocyte-Count,** these

[1] From work by Andrewes (Croonian Lectures, *Lancet,* 1910) and others, it appears that the distribution of the leucocytes, particularly the polymorphs, is by no means uniform throughout the circulating blood in the different organs and tissues of the body. Thus, apart from the bone-marrow, they are found in very

must be carefully compared with the **Total Leucocyte-Count;** and, if necessary, the **Relative Absolute Numbers of each Variety of Leucocyte per c.mm.** must be calculated—otherwise a very erroneous impression may be given by the figures of the relative percentage count alone.

A detailed description of the various forms of leucocytes is given in the Chapter on **Inflammation** (*see* pp. 174 *et seq.*), but it is convenient to repeat this description here. Reference should also be made to Plates IV, V, VI, VII, VIII, XIII, and XV.

i. **Polymorphonuclear Leucocytes.**—These leucocytes are the commonest variety in the blood, in which they constitute about seventy per cent. of the total leucocytes. They have a nucleus which is divided into segments or lobes, each segment being connected by means of a delicate filament of chromatin. The number of these lobes has been observed to be increased in certain toxic conditions, and such variations are considered by some writers to have a certain diagnostic and prognostic value, for example, in tuberculosis.[1] Carnegie Dickson has noted great exaggeration in the complexity of the polymorph nucleus under the experimental action of snake-venom, whilst thyroid extract also appears to have a certain action in this direction. The cytoplasm contains irregularly scattered, fine granules which stain faintly with eosin. As has already been noted, these leucocytes are actively amœboid and phagocytic. In the process of phagocytosis, they are specially concerned with the destruction of bacteria; and, from the fact that they are smaller than the other actively phagocytic cells of the blood, viz. the large mononuclear cells, they have been termed the **microphages** by Metchnikoff. In the majority of bacterial infections, these cells are increased in number, the condition being termed a **polymorphonuclear leucocytosis,** or—from the fact that it is usually produced by more or less acute bacterial infections—**inflammatory leucocytosis** or **leucocytosis** proper. Variations in the number and staining-reactions of the granules occur in certain pathological conditions. They may be scanty in cases where the cells are being rapidly produced, *e.g.* in excessive or prolonged polymorph leucocytosis, myelogenous leukæmia, etc. (*see* p. 610).

ii. **Coarsely Granular Eosinophils.**—These cells are usually stated to constitute from one to three, or even four, per cent. of the white corpuscles of normal blood. In the experience of the authors, the average is usually about one to one-and-a-half per cent. When stained with eosin, they show in their protoplasm brilliantly-coloured

large numbers in the spleen-pulp (where they probably undergo destruction when effete), and also in large numbers in the lung-capillaries. In the liver, they are fairly numerous, less so in the kidney, and, in some organs such as the brain, they appear to be comparatively scanty. The facts given by Andrewes are of interest, as the study of the phenomena of leucocytosis, etc., clinically, is usually based upon the examination of the *peripheral* blood, only.

[1] *See* pp. 600–1, for a note on these changes in Leucocytosis, the Arneth-Count, etc.

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pink granules, which are much larger and more highly refractile, than those in the polymorphonuclear leucocytes. The lobed character of the nucleus is not so marked, and it stains less intensely with the basic dyes. These cells are very fragile, and readily break down and discharge their granules. In certain conditions, especially in diseases due to animal parasites, they may be very markedly increased in number (*see* p. 602).

The **Mononucleated Leucocytes.**—These cells, as they occur in the blood, may be divided thus :—

iii. **Lymphocytes.**—These vary in size. Many are comparatively **small** cells—about the size of a red corpuscle or slightly larger—with a relatively large, darkly-staining nucleus, and with very scanty cytoplasm, in which a few small basophil granules can usually be seen near the periphery. Others are larger cells similar to those described, but having more abundant cytoplasm (**the large lymphocytes**), all sizes between the typical small, and the typical large, lymphocyte being also found. The relative numbers of small and large lymphocytes vary very much in individual cases, but the significance of such variations is not yet fully understood. These together constitute from about twenty-five to forty-five per cent. of the colourless corpuscles of the blood.

iv. **Hyaline Leucocytes,** or **Large Mononucleated Cells,** are present in small numbers in the circulating blood, but are more abundant in certain pathological states, *e. g.* malaria. In their general character, they resemble the large lymphocytes, and it is often very difficult to draw any absolute distinction between them. They are generally described as having an oval or kidney-shaped nucleus which stains less intensely than that of the lymphocytes, and cytoplasm which is devoid of granules. This distinction, however, cannot be definitely maintained, as intermediate forms are frequently present. Certain observers hold that transition forms between the lymphocytes, small and large, and these hyaline cells can be seen in the blood, and that one is derived from the other. This certainly is not in accord with our observations. In malaria, where there is a great increase of the " **hyaline** " leucocytes, the ordinary lymphocytes may not be proportionally increased; and, in other cases, where the small lymphocytes are greatly increased in number, there need not be any increase in these large mononuclear cells. This would certainly suggest that the two kinds are distinct in origin. It is, we think, not improbable that some of these large mononuclear cells may originate from vascular and lymphatic endothelium. In regard to migration, there is now abundant evidence that the lymphocytes can migrate. The large mononuclear cells shew well-marked amoeboid movements on the warm stage, and are able to pass out of the vessels in virtue of this property.

v. **Mast-Cells,** about a half per cent. of the leucocytes, are characterised by the presence of irregularly scattered, larger and smaller basophil granules, or granules which shew metachromatic staining. These cells are more frequent in some pathological conditions of the blood, *e. g.*

myeloid leukæmia. The view that mast-cells are degeneration products of other cells has recently gained ground and is probably correct, as, in certain exudates, all intermediate stages can be observed between the ordinary polymorph (and perhaps other varieties of cell) and the typical mast-cell.

Abnormal Forms of White Cells occurring in pathological blood will be discussed after the origin of the various blood-cells has been described.

C. BLOOD-PLATES OR -PLATELETS

The nature and origin of these bodies are as yet but little understood. They are small, rounded or somewhat oval, extremely adhesive structures, about two or three micro-millimetres in diameter. They do not stain well with the ordinary dyes, and are best seen in preparations which are **rapidly** made, and fixed and stained by some modification of the **Romanowsky method,** e. g. that of Leishman or of Jenner. When so prepared, they consist of a clearer, homogeneous peripheral part, with a darker, sometimes rather granular, red-staining centre. They are said to be composed mainly of nucleo-proteins. Their origin is much disputed, some holding that they are of the nature of extrusions from the red cells (Ewing, Maximow, Klebs, Arnold, and others); whilst some authorities are of opinion that they are derived from the nuclei of leucocytes; and others, again, from a study of very carefully stained preparations, believe them to be produced by the giant-cells of the marrow (Homer Wright). The older view, now practically discarded, was that they were of the nature of precipitation-products in the plasma. They play an extremely important part **in the formation of thrombi,** collecting around, and adhering with great readiness to, foreign bodies in the blood-stream, or to injured areas on the walls of the blood-vessels or of the heart. They are the chief components of **vegetations** occurring on the heart-valves, and have, owing to these properties, sometimes been termed **thrombocytes.** They probably contain the thrombokinase. which, in the presence of calcium salts, converts prothrombin into thrombin or fibrin-ferment.

The determination of their precise number in the blood is a matter of considerable difficulty, but it is probable that, in health, they vary between 200,000 and 500,000, the average being about 250,000 per cubic millimetre. Pathologically, though the recorded results are somewhat contradictory, they appear to be increased in numbers after hæmorrhage, in pneumonia, in leucocythæmias, and in many anæmic conditions; whilst they are diminished, as a rule, in typhoid and many other acute fevers, purpura, hæmophilia and in malaria. In pernicious anæmia they are usually, though not always, decreased in number.

ORIGIN AND FORMATION OF BLOOD-CELLS

The probable part played by the **endothelial cells** lining vascular channels, lymphatics, and serous surfaces, in the formation of **large**

mononucleated cells of the blood, is discussed in the Chapter on **Inflammation** (pp. 178 and 183).

Apart from these cells, however, in extra-uterine life, the majority of the formed elements originate **in the bone-marrow;** but the **lymphatic glands** and the **adenoid tissue** of the spleen, intestine, omentum, etc., must also be regarded as important hæmopoietic tissues.

A short description of the physiology and pathology of these tissues is, therefore, necessary at this point.

I. LYMPHOID TISSUE OF LYMPHATIC GLANDS, SPLEEN, INTESTINE, OMENTUM, ETC.

The histology of lymphoid tissue is sufficiently described in standard textbooks on Histology, and a very brief *résumé* will, therefore, suffice for our purpose. Such lymphoid tissue consists of an **adenoid reticulum,** made up, partly of the branching and interlacing processes of its cells, and partly of formed connective-tissue fibrils. In the interstices of this reticulum, which is richly supplied with blood-vessels, are situated the closely-packed **lymphoid cells**—mostly small lymphocytes with scanty protoplasm and relatively large, darkly-staining nuclei. Such lymphoid tissue is present in the lymphatic glands, in the solitary and agminated glands of the intestine, in the tonsils, Malpighian bodies of the spleen, and in the omentum, mesentery, etc. It is also found in the thymus gland before the occurrence of the atrophy by which that gland is more or less completely transformed into adipose tissue. (*See* p. 630 and fig. 283: and p. 847.)

II. BONE-MARROW [1]

It is convenient to describe first the **varieties of bone-marrow;** then to enumerate the different **varieties of cell** which may be found in the tissue; next to deal with the most important **reactions** and **degenerations** to which it is liable under pathological conditions; after which to briefly recapitulate the more important of the known **functions** of the tissue.

(A) VARIETIES OF BONE-MARROW

(See Plate XV and Figs. 267 to 280.)

(1) **Primitive or Embryonic Marrow.**—The medullary cavities of the bones are, early in development, filled with a tissue composed of cells, mucoid or "myxomatous" in type, possessing numerous branching and interlacing processes. These are, in histological structure and appearance, similar to the cells found in other mucoid tissues in the fœtus; and, in this situation, they afterwards develop into the **adenoid reticulum** or connective-tissue framework of the marrow, in the interstices of which

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[1] This *résumé* was originally published by one of the authors (W. E. Carnegie Dickson) in *International Clinics*, vol. ii., seventeenth series, J. B. Lippincott Company, 1907, p. 299. It is reproduced here with the kind permission of the Editors and Publishers of that periodical.

DESCRIPTION OF PLATE XV

PLATE XV

NAKED-EYE APPEARANCE OF THE BONE-MARROW IN VARIOUS ACUTE DISEASES

(These illustrations are from the upper portions of the shaft of the Femur, except No. 2, which is from the upper part of the humerus)

1. From a case of ACUTE LOBAR PNEUMONIA accompanied by LEUCOPENIA (male, aged 41), illustrating the practically complete absence of any leucoblastic reaction on the part of the bone-marrow, and accounting for the non-appearance of leucocytosis in this case, the disease progressing rapidly to a fatal termination. Only a trifling amount of congestion is shewn in these sections.

2. From a case of ACUTE LOBAR PNEUMONIA accompanied by LEUCOPENIA (female, aged 65) shewing the same condition as the foregoing specimen. Note the very small areas of incomplete leucoblastic transformation. The marrow is practically fatty throughout.

3. From a case of ACUTE LOBAR PNEUMONIA of five days' duration (male, aged 48), illustrating the earlier stages of LEUCOBLASTIC TRANSFORMATION in acute disease characterised by POLYMORPHONUCLEAR LEUCOCYTOSIS. A considerable amount of fat is still present, and the red reaction is seen spreading inwards from the periphery. The cancellated bone has as yet undergone only partial absorption.

4. From a case of RHEUMATIC PERICARDITIS of 14 days' duration (female, aged 14). The condition was accompanied by well-marked POLYMORPHONUCLEAR LEUCOCYTOSIS. The LEUCOBLASTIC TRANSFORMATION is passing inwards from the periphery, and the cancellated bone is undergoing absorption.

5. From a case of SEPTIC PERITONITIS of three days' duration due to PERFORATED GASTRIC ULCER (female, aged 24). The medullary cavity has not yet had time to enlarge by process of bone-absorption, though the smaller trabeculae towards the central part have disappeared. The marrow has a diffuse, slightly mottled, dark red appearance due to engorgement of the venous sinuses and capillaries and to a diffuse network of leucoblastic tissue. Note the area of fatty tissue at the lower part of the figure, i.e. the central part of the shaft, where the transformation from yellow to red marrow is last to occur.

6. From a case of CHRONIC SEPTICÆMIA of about a year's duration. Upon the long-continued LEUCOBLASTIC REACTION, exhaustion of the tissue had supervened, as evidenced microscopically by the commencement of gelatinous degeneration. The leucoblastic reaction is now being replaced by an erythroblastic one due to the presence of the secondary anæmia caused by the long continuation of the disease, as well as to the exhaustion of the leucoblastic functions of the marrow. From the lower part of the longitudinal section the marrow has been removed by washing, in order to demonstrate the absorption of the cancellated bone and partial erosion of the compact bony walls of the medullary cavity. The oblique entrance of the medullary artery is also shewn.

Plate XV. Vol. II.
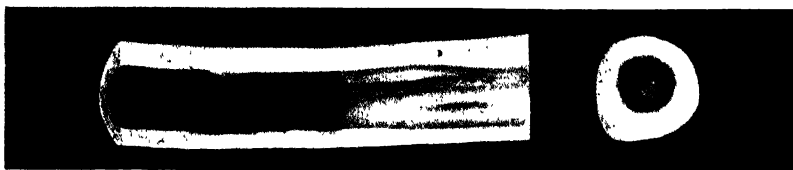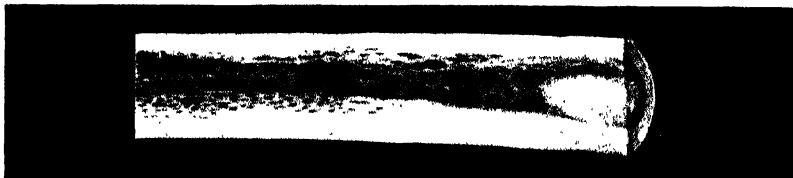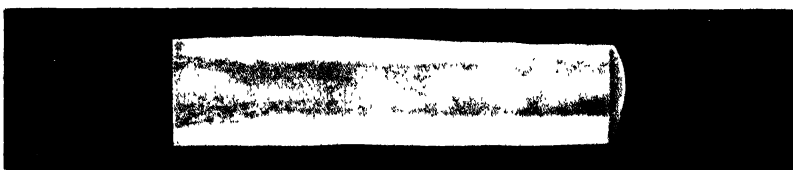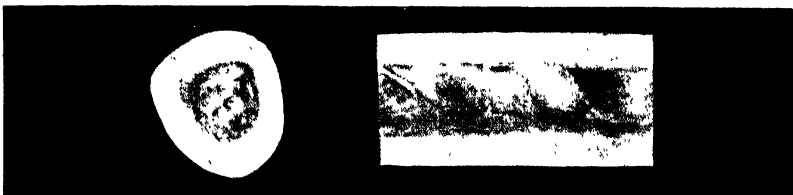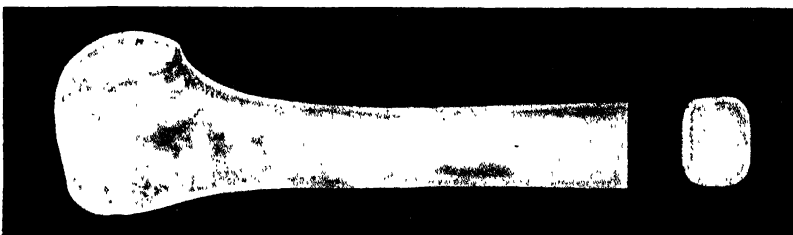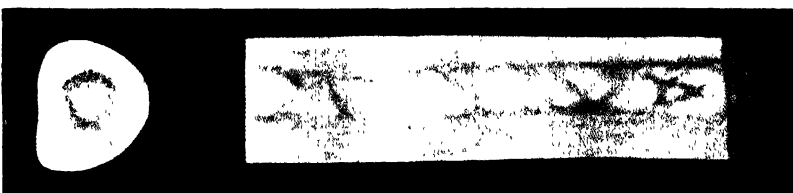
appear, about the fourth month of fœtal life or a little earlier, the **hæmo-poietic cells proper.** By the proliferation of these cells is formed the next variety of marrow.

(2) **Red, " Lymphoid," or Formative Bone-Marrow** proper, in which, except during fœtal, and perhaps early infant, life when the liver and spleen still retain some of their primitive hæmopoietic functions, are developed all the **red blood-corpuscles, the majority, if not all, of the granular leucocytes,** and possibly also some of the **non-granular white cells** of the blood.

In the infant and young child, this type of marrow is found throughout the interior of the entire osseous system, but, as age advances, in certain situations, especially within the central parts of the shafts of the long bones, the red marrow tends to undergo a process of physiological " degradation." the hæmbpoietic cells almost entirely disappearing from large tracts of the tissue, and the space being filled by a development of fat within the connective-tissue cells of the adenoid reticulum. (*See* fig. 277.) Usually, however, **some** of the blood-forming cells remain towards the periphery of the shaft, and also more especially towards the ends of the long bones, a point of extreme importance, as will be seen later, from the fact that it is from these positions that proliferation may again take place should there be any special demand for increased production of blood-cells. In the short, flat and irregular bones, especially in the sternum, ribs, vertebræ, and cranial bones, the red marrow undergoes a much less degree of this fatty change ; though, even in these situations, there is a progressive increase in its amount, which may become very considerable in advanced age and in some pathological conditions. There is, therefore, in the red, as well as in the fatty, marrow, a potentiality for the proliferation of the blood-forming elements, and for a corresponding diminution or absorption of the fat-cells, should there be a necessity for increased output of the blood-cells formed in the marrow (*see* Plate XV, and figs. 269 to 279).

(3) **Yellow or Fatty Marrow.**—This variety of marrow is found as age advances, more especially in the central parts of the shafts of the long bones, as above described, the fat being developed within the cells of the adenoid reticulum. These areas of fatty marrow form a most important " **potential area** " in which the development of blood-forming cells can be carried on, should there be any special call for these cells to combat the attack of disease, or to replace cells destroyed by its action, for example, in many of the acute and chronic diseases characterised by leucocytosis, or by anæmia. Any factors interfering with this reaction, *e. g.* chronic degenerative conditions of the marrow such as may be found in syphilis, chronic alcoholism, lead-poisoning, malignant disease, the prolonged action of X-rays, etc., may lead to a rapidly fatal issue if a patient so affected contracts an acute febrile disease such as pneumonia. Two of the most important of such degenerative conditions of the marrow may next be described.

(4) **Fibroid and Sclerotic Marrow.**—In old persons, or earlier in life under certain pathological conditions, and more especially in syphilis,
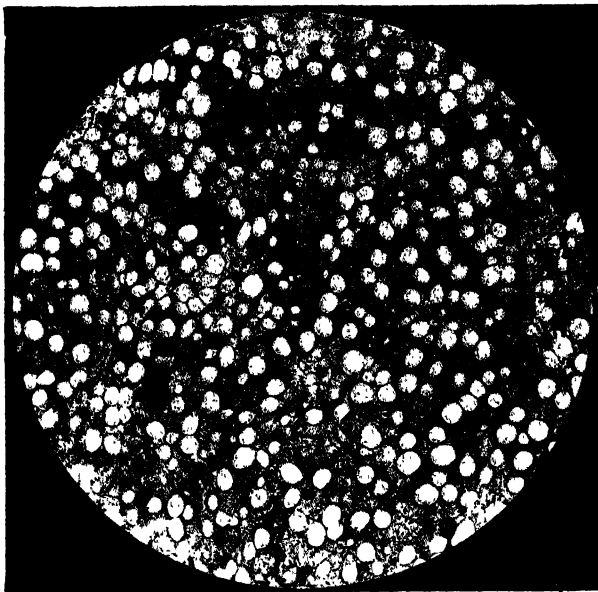
FIG. 267.—Transverse Section of Marrow of Femur from a case of carcinoma of the intestine, shewing the more usually described variety of gelatinous degeneration, a chronic condition supervening in old-standing disease, especially associated with cachexias and states of inanition, and often occurring after prolonged leucoblastic or other excessive forms of marrow-activity.

The " gelatinous " material is formed by transformation of the fat-cells and reticulum, with progressive disappearance of the hæmopoietic tissue.   ×45.
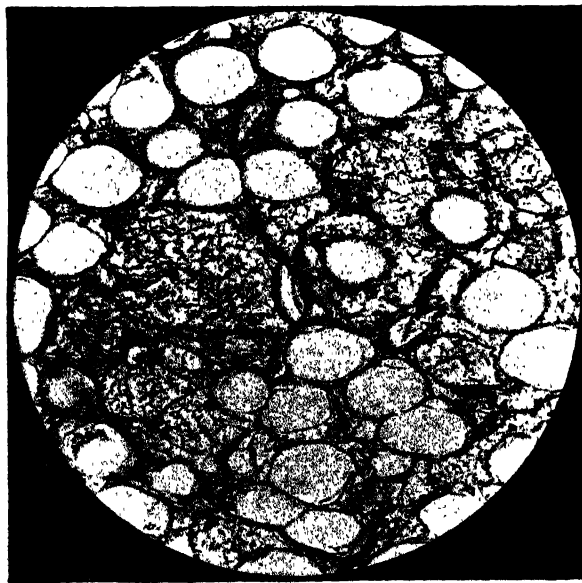
FIG. 268.—Transverse Section of Marrow of Femur from a case of ulcerative endocarditis of three weeks' duration, shewing high-power view of the more acute form of gelatinous degeneration. The fat is undergoing absorption, the cytoplasm of the fat-cells showing mucoid degeneration. Blood-forming cells are entirely absent. ×200.

the connective-tissue elements may be found proliferating at the expense of the more highly endowed, and therefore more delicate and more easily destroyed, functioning cells of the part.. This change may be due to the direct action of some toxic substances, as well as to diminished nutrition from vascular and other derangements. Ossification, partial or complete, may supervene, and the bones may become unduly dense, as in syphilis; whilst, in other cases, the bony tissue may become partially absorbed and unduly porous (*see under* **Diseases of Bone,** p. 1034).

(5) **Gelatinous Marrow.**—This is an important degenerative change, which may supervene in old age, and especially in cases of chronic debilitating disease accompanied by anæmia, such as cancer, phthisis, etc., or in starvation (*see* fig. 267). It may also occur very rapidly in acute diseases such as ulcerative endocarditis, pneumonia, puerperal and other forms of septicæmia, diphtheria, etc., where the organisms or their toxins possess a high degree of virulence (*see* fig. 268).

Gelatinous degeneration may attack both yellow and red marrow, and seems specially liable to be found when they have previously undergone prolonged leucoblastic transformation and where the proliferative changes have not been kept up, *i. e.* in exhaustion supervening in an overactive marrow in which the strain cannot be maintained (*see* Plate XV, fig. 6). It is important also to bear in mind that the condition can be brought about **artificially** by certain drugs, which, at first, when given in small therapeutic doses. may stimulate the hæmopoietic functions of the marrow, *e. g.* arsenic, lead, mercury, etc.; but the prolonged application or excessive doses of which may bring about profound gelatinous degeneration, accompanied by complete disappearance of the blood-forming cells from large tracts of marrow-tissue.

(B) VARIETIES OF CELL FOUND IN THE MARROW

Only a bare enumeration of the cells found in the marrow is possible in a short *résumé* of the subject such as this.[1] In film-preparations and in sections of red or blood-forming bone-marrow, the following varieties of cells may be distinguished (*see* Plate XVI, figs. 3 and 4) :—

I. BLOOD-FORMING CELLS.

A. **LEUCOCYTE-SERIES :—**

(*a*) **Non-granular cells** with basophilic protoplasm :—

    1. **Large.**

    2. **Small.**

        i. Cells similar to, but smaller than, the large variety.

        ii. Cells identical with the small lymphocytes of the blood in appearance and in staining reactions.

[1] For a more detailed account of these, *see* " The Bone-Marrow : A Cytological Study forming an Introduction to the Normal and Pathological Histology of the Tissue, more especially with regard to Blood-Formation, Blood-Destruction, etc.," by W. E. Carnegie Dickson. Longmans, Green & Co., London, 1908. From this monograph, Plate XV, and figs. 267 to 280 are taken.

(*b*) **Granular cells :—**

    1. **Neutrophil** (corresponding to **amphophil** in the rabbit) :—
        i. Myelocytes, with large, rounded or oval nucleus.
            (*a*) Larger variety.
            (*b*) Smaller variety.
        ii. Intermediate cells, with indented or horseshoe-shaped nucleus.
        iii. Polymorphonuclear cells, or fully-developed leucocytes.
    (These cells form a complete developmental series of cells gradually merging into one another, *see* p. 600.)

    2. **Eosinophil :—**
        i. Myelocytes.
        ii. Intermediate cells.
        iii. Polymorphonuclear cells or leucocytes.

    3. **Basophil :—**
        (*a*) Mast-cells.
            i. Myelocytes.
            ii. Intermediate cells.
            iii. Polymorphonuclear cells.
        (*b*) Cells resembling the eosinophil myelocytes but with granulations staining with the basic dye.

B. HÆMOGLOBIN-HOLDING SERIES :—

    1. **Normoblasts,** developing into **normocytes** or ordinary red blood-corpuscles.
    2. **Megaloblasts,** normally giving rise, in the fœtus, to **normoblasts,** or, under certain pathological circumstances, *e. g.* in pernicious anæmia, producing **Megalocytes** (*see* p. 620).
    3. **Gigantoblasts,** developing into **Gigantocytes,** these being merely very large forms of the preceding variety of cell, found especially in pernicious anæmia (p. 620).

II. GIANT-CELLS:

    1. **Mononucleated.—Megakaryocytes,** with single, highly complex, basket-like nucleus.
    2. **Multinucleated.—Polykaryocytes,** *e. g.* osteoclasts, etc.

III. CELLS OF CONNECTIVE-TISSUE TYPE.

    1. **Fat-Cells.**
    2. **Cells** of the **Adenoid Reticulum.**
    3. Various forms of **Phagocytic Cell** (pigmented cells, etc.).
    4. Ordinary **Connective-Tissue Cells** passing in with blood-vessels, etc.

IV. ENDOTHELIAL CELLS.

(Lining the walls of capillaries, blood-sinuses, etc.)

    1. Found in their **normal** positions in the vessel-walls.
    2. Found **proliferating,** taking on phagocytic functions, etc.
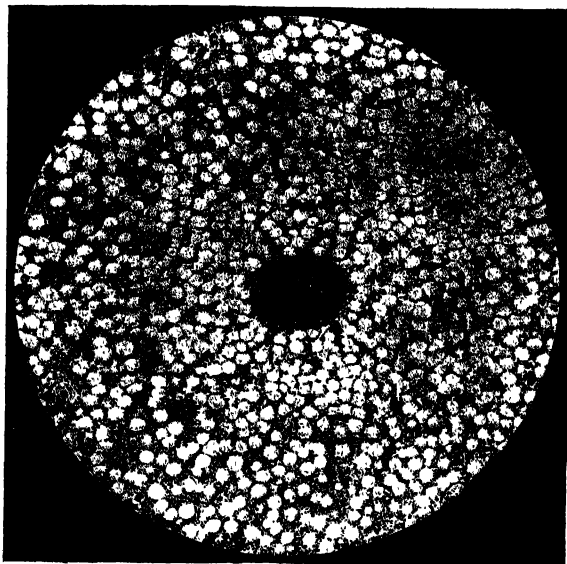
FIG. 269.—Transverse Section of Bone-Marrow from Femur of healthy Rabbit, shewing the average normal proportions of fatty and cellular tissue. Note central venous sinus, a thin-walled vascular space, into which run venous-capillary channels which pass in radially from the periphery towards the centre of the marrow. (Cf. fig. 270, in which these vascular spaces are congested, and therefore shew more clearly.) ×45.
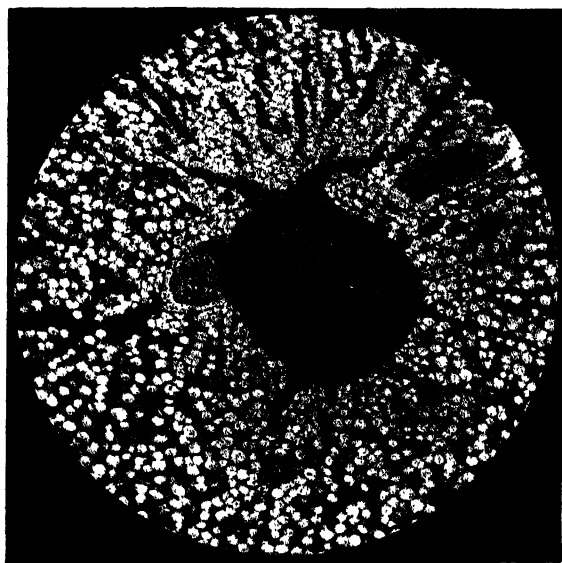
FIG. 270.—Transverse Section of Bone-Marrow from Femur of Rabbit inoculated with pus from pneumococcal empyema (death in 18 hours), shewing congestion of central venous sinus and tributary venous-capillary channels. The medullary artery and some of its branches are also seen in the section. The fat is already slightly diminished, but little proliferation of the hæmopoietic cells has yet had time to occur. ×45.
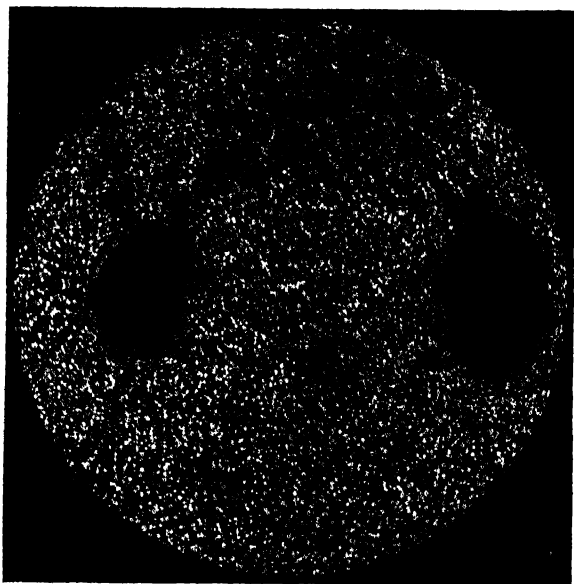
Fig. 271.—Transverse Section of Bone-Marrow from Femur of Rabbit, inoculated with diphtheria toxin (5 M.L.D.) (death in 33 hours), shewing very intense congestion of the two main tributaries of the central venous sinus and venous-capillary channels. The amount of fat is now greatly diminished, and there is marked proliferation of the blood-forming tissue, corresponding to the leucocytosis observed clinically.   × 45.
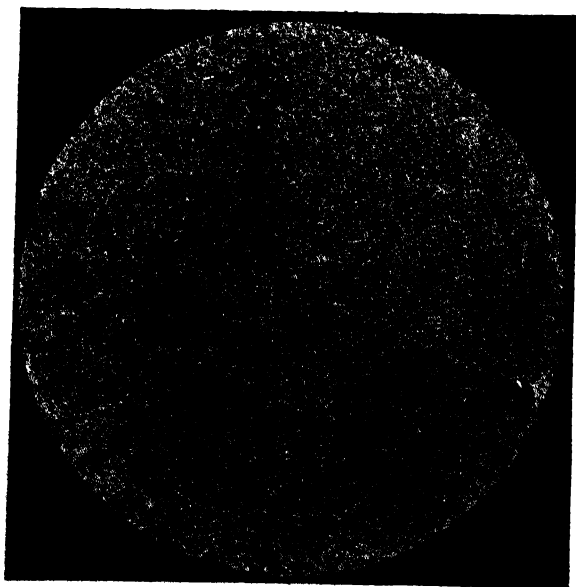
Fig. 272.—Transverse Section of Bone-Marrow from Femur of Rabbit, inoculated with sputum from case of pneumonia containing *Pneumococci* of diminished virulence (death in 10 days), shewing complete leucoblastic transformation, with total disappearance of the fat-cells.   × 45.
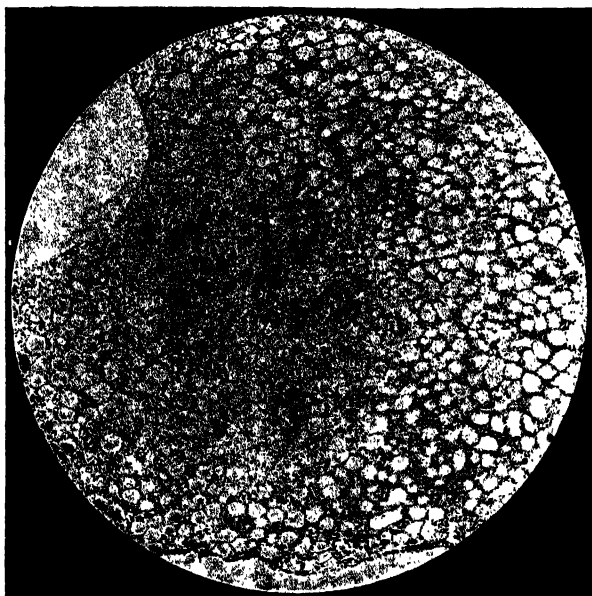
FIG. 273.—Section of normal Rib-Marrow from the human subject, shewing relative amounts of fatty and blood-forming tissue. ×45.
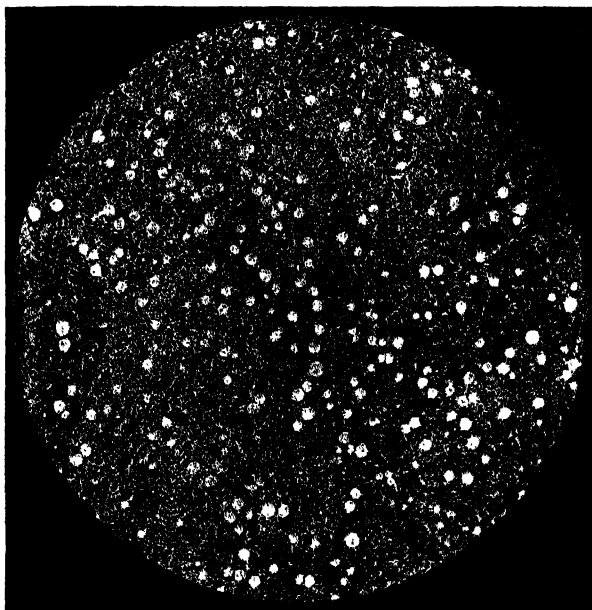
FIG. 274.—Section of human Rib-Marrow from a case of rheumatic pericarditis with leuco-cytosis, shewing comparatively complete leucoblastic transformation, combined (as could be determined when examined under a higher magnification) with a considerable degree of erythroblastic change, corresponding to a certain degree of anæmia. Note the few scattered fat-cells of small size still remaining. ×45.
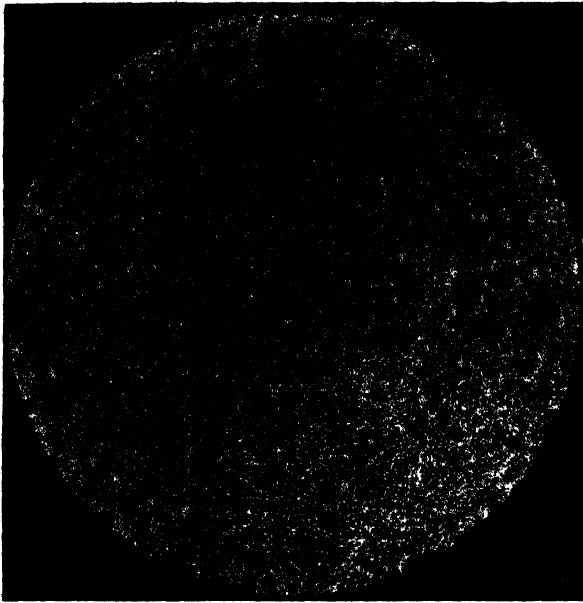
Fig. 275.—Section of human Rib-Marrow from a case of chronic septicæmia, shewing almost complete disappearance of fat-cells. Under a higher magnification the change is largely erythroblastic, this condition having supervened upon a long-standing leucoblastic reaction with exhaustion of the marrow, and anæmia.   ×45.
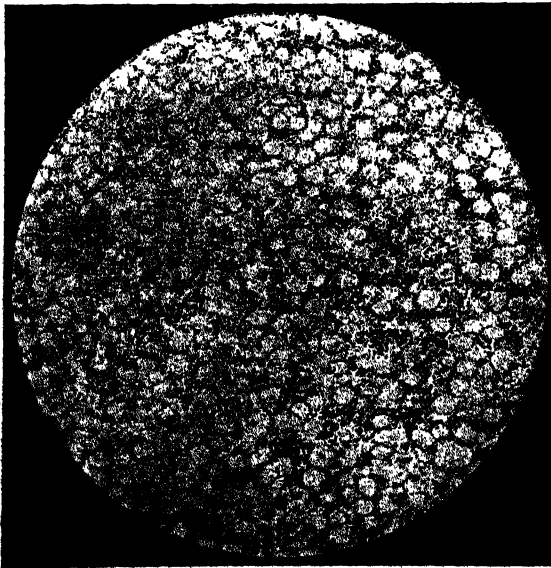
Fig. 276.—Section of human Rib-Marrow from a case of pneumonia with leucopenia, shewing that the defective leucocytosis was due to non-reaction of the blood-forming marrow-tissue. Compare with figs. 273, 274, and 275.   ×45.
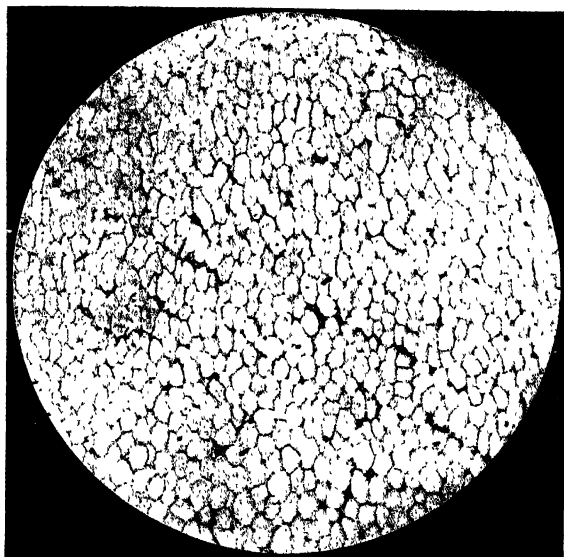
FIG. 277.—Transverse Section of Bone-Marrow of human Femur to shew normal appear-
ance of yellow marrow in centre of a long bone. Note the almost complete
absence of blood-forming cells—only a few small groups being seen. ×45.
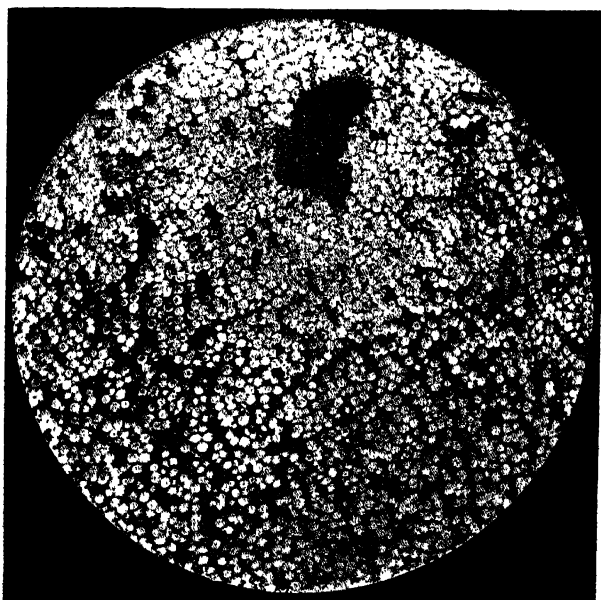
FIG. 278.—A similar section of the Marrow of the Femur from a case of streptococcal
septicæmia to illustrate leucoblastic change spreading in from the periphery. The
central venous sinus and the accompanying medullary artery are seen towards the
upper part of the section. ×45.
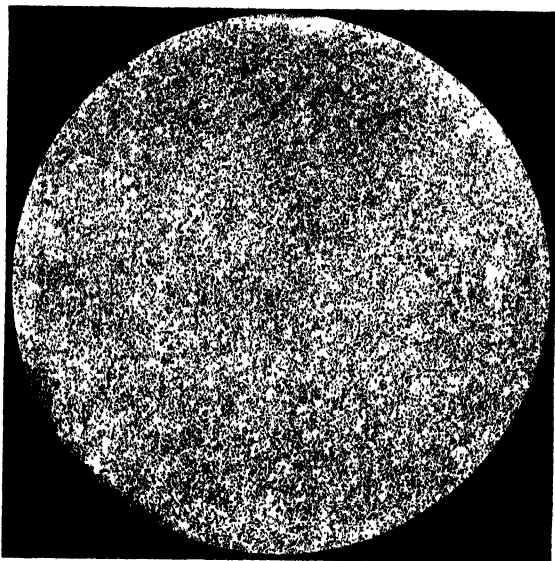
FIG. 279.—A similar section of the Marrow of the Femur from a case of chronic staphylococcal abscesses of six months' duration, the fatty marrow being completely transformed into active blood-forming tissue. ×45.
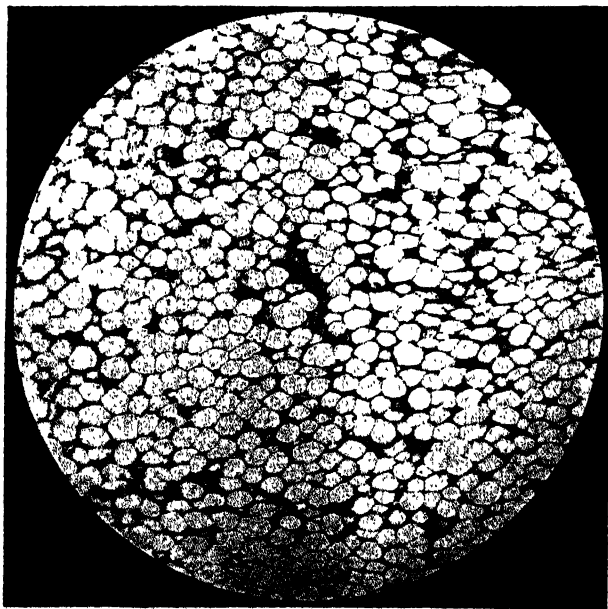
FIG. 280.—Transverse Section of Marrow of Femur from a case of pneumonia with leucopenia, to show defective leucoblastic reaction. The cellular areas seen are largely engorged capillaries with very little leucoblastic change. ×45.

[Figs. 267 to 280 are borrowed from Carnegie Dickson's "The Bone-Marrow: A Cytological Study," Longmans, Green & Co., London, 1908.]

(C) REACTIONS OF THE BONE-MARROW IN DISEASE

(See Plate XV, figs. 269 to 280.)

In many diseased conditions, rapid proliferative changes may occur both in the red, and in the yellow, marrow, and, according as the change is characterised by the increased production of **red**, or of **white, blood-cells,** the process may be described as being either **erythroblastic or-leucoblastic** in type. In health, there is, in the marrow, a normal balance between these two processes; and, usually, when the tissue is first stimulated to proliferate, there is increased production of **all varieties** of marrow-formed blood-cells. Soon, however, in most cases, the tissue is found to produce more particularly the variety of cell for which there is special demand, and the reaction becomes either **leuco-** or **erythro-blastic in type,** though, in some cases, **both** changes may occur simultaneously in the same marrow. A very common sequence of events which may be found in certain chronic septicæmias and other diseases is, first of all, with the occurrence of a polymorphonuclear leucocytosis, a slight transitory increase in the number of red cells in the peripheral blood. Then, if the leucocytosis has to be kept up for a prolonged period, the reds become progressively diminished in numbers. If the marrow be examined, corresponding phenomena will be found occurring, i. e. the leucoblastic will now predominate over, and obscure, the erythroblastic type of reaction; and, if the leucocytosis has to be maintained for a still longer period, degenerative changes may occur in the leucoblastic marrow, and a progressive anæmia, characterised by transformation to the erythroblastic type of reaction, may supervene. Then, as the anæmia becomes more profound, this too may pass off as exhaustion of the marrow supervenes, and the blood-forming tissue may undergo gelatinous degeneration.

LEUCOBLASTIC MARROWS.—Corresponding roughly with the different types of leucocytosis observed clinically, we may subdivide the leucoblastic changes found in the marrow into four groups, several of these being often more or less combined in any given case :—

(1) **Neutrophil leucoblastic reaction** (see Plate XV, figs. 3, 4 and 5). This type is found especially in connection with the establishment of an **inflammatory leucocytosis,** i. e. an increased production of the neutrophil series of cells, a condition found in the majority of acute infective diseases, whether these be **local** (e. g. inflammation, abscess-formation, etc., due to the presence of Staphylo- and Strepto-cocci, B. coli, and many other micro-organisms), or more **general conditions,** such as pneumonia, the septicæmias, etc. The results produced in the marrow are practically identical in both sets of cases, differing rather because of the intensity, quality, and amount of the irritant, than on account of its special point of attack and distribution in the body. This leucoblastic reaction is, of course, naturally most readily produced **in the red marrow** (see figs. 274 and 275), and shews as an increased proliferation of the special variety of hæmopoietic cell

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required—in this case the neutrophil myelocytes. But, if further demands are made upon the tissue, the change spreads **into the fatty or yellow marrow** in the shafts of the long bones and elsewhere (*see* figs.278 and 279); and, in these situations, all degrees of the reaction may be observed, up to complete transformation to fully formed red marrow. In the case of the long bones, this transformation is found to spread into the fatty marrow **from the periphery and ends of the shaft,** *i. e.* from the situations in which the hæmopoietic cells have not completely disappeared as the physiological degradation of the marrow to fatty tissue occurs. Any pathological conditions preventing this leucoblastic reaction on the part of the marrow, *e. g.* the presence of fibroid or gelatinous degeneration (*see* figs. 267 and 268), may determine a rapidly fatal issue in a case, say, of pneumonia, diphtheria, etc.; and such cases may thus be characterised clinically by the **absence of leucocytosis (aleucocytosis),** or even by **hypoleucocytosis** or **leucopenia,** *i. e.* diminution of the leucocyte-count (*see* p. 601 and 603).

(2) **Eosinophil leucoblastic reaction.**—Characterised by special increase of the eosinophil granular cells.

(3) **Basophil leucoblastic reaction.**—Characterised by special proliferation of the basophil granular cells (mast-cells), a condition found, along with other changes, particularly in myelogenous leukæmia, and in certain nutritional disorders.

(4) **Hyaline leucoblastic reaction.**—Characterised by an increase in the numbers of the pre-myelocytes or myeloblasts, *i. e.* large basophil non-granular cells from which the granular series are developed. This type of reaction is specially found in marrows from cases of prolonged leucocytosis, *e. g.* in chronic septicæmias or pyæmias, malignant disease, etc., and, in its most extreme form, is observed in cases of so-called acute " lymphatic " leukæmia.

ERYTHROBLASTIC or **RED BLOOD-CELL-FORMING MARROWS** may be subdivided into two main types :—

(1) **Normoblastic**—*i. e.* marrows in which normoblasts or normal nucleated red cells are found in excess, *e. g.* after hæmorrhage, and in most secondary anæmias, where the tissue endeavours to compensate for the deficiency in the number of the red corpuscles of the blood. The fact has already been noted that this change may also supervene in leucoblastic marrows which have become exhausted.

(2) **Megaloblastic**—where a more primitive type of red cell-formation is developed. Megaloblasts—or nucleated red cells of abnormally large size,[1] and possessing nuclei of more primitive type—are increased in number in the marrow in various diseases, both acute and chronic. They are usually present only in small numbers, although in some cases of exophthalmic goître, malignant disease, tuberculous disease, many acute and

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[1] Note.—For the classification of these cells, the primitive character of the nucleus is of much greater significance than the mere size of the cell.

DESCRIPTION OF PLATE XVI˙

PLATE XVI

FIG. 1.—*Blood-Film from a case of Pernicious Anæmia* (stained with eosin and methylene-blue). × 500

    a.—Polymorphonuclear leucocyte.
    b.b.—Normocytes.
    c.c.—Various erythrocytes shewing polychromatophilia, or diffuse basophilia.
    d.—Normocyte shewing punctate basophilia.
    e.—Normoblast.
    f.—Normoblast shewing karyorrhexis *f'.f'.* Nucleated red corpuscles, more or less intermediate between normo- and megalo-blasts, also shewing karyorrhexis.
    g.—Normoblast shewing punctate basophilia.
    h.—Megalocyte.
    i.—Megaloblast.
    j.—Megaloblast shewing karyorrhexis.
    k.—Megaloblast shewing punctate basophilia.
    l.l.—Microcytes (some probably formed by fragmentation of larger cells).
    m.m.—Poikilocytes.

FIG. 2.—*Blood-Film from a case of Chlorosis* (stained with Leishman's stain). The red cells are poor in hæmoglobin, and shew pallor of their centres. × 500

    a.—Polymorphonuclear leucocyte.
    b.—Lymphocyte.
    c.—Normoblast.
    d.—Blood-platelets.

FIG. 3.—*Bone-Marrow Film (Rib) from a case of Pneumococcal Empyema, shewing Leuco-blastic Reaction* (stained with eosin and methylene-blue). × 500

    a.a.—Adult polymorphonuclear neutrophil leucocytes.
    b.b.—Immature polymorphonuclear neutrophil leucocytes.
    c.c.—Intermediate neutrophil myelocytes.
    d.d.—Neutrophil myelocytes.
    d'.d".d'".—Neutrophil myelocytes shewing stages of karyokinesis.
    e.e.—Non-granular cells, possibly pre-myelocytes, *i. e.* parent-cells of the granular myelocytes.
    f.—Coarsely-granular polymorphonuclear eosinophil leucocyte.
    g.g.—Coarsely-granular eosinophil myelocytes.
    h.h.—Small lymphocyte-like cells.
    i.i.—Normoblasts.

FIG. 4.—*Bone-Marrow Film (Femur) from a case of Pernicious Anæmia, shewing an Erythroblastic Reaction of Megaloblastic type* (stained with eosin and methylene-blue). × 500

    a.a.—Neutrophil myelocytes.
    b.—Coarsely-granular polymorphonuclear eosinophil leucocyte.
    c.c.—Coarsely-granular eosinophil myelocytes.
    d.d.—Normocytes.
    e.e.—Normoblasts shewing karyolysis, karyorrhexis, poikilocytosis, etc.
    f.f.—Megaloblasts shewing similar changes (note that all transitions are found between normoblasts and megaloblasts; hence there is often difficulty in classifying individual cells).
    g.—Megaloblast with typical "primitive" type of nucleus.

chronic septic conditions, typhoid fever, etc., they have been observed with comparative frequency, and sometimes in large numbers.[1] The most extreme degree of megaloblastic transformation, however, is seen in cases of pernicious anæmia (see Plate XVI, fig. 4), and in certain secondary anæmias closely allied to it, notably in those due to the presence of *Dibothriocephalus latus, Ankylostoma duodenale* and other intestinal parasites, and also in myelogenous leukæmia.

In the **aplastic anæmias,** which may be **congenital** or **acquired,** the erythroblastic power of the marrow is diminished or lost. Prolonged exposure to the more penetrating varieties of X-rays may bring about this condition.

(D) FUNCTIONS OF THE BONE-MARROW

These may be briefly summarised as follows :—

(1) **Hæmopoietic Functions.**

    (a) **Erythroblastic.**—The formation of red blood-cells.

    (b) **Leucoblastic.**—The formation of white blood-cells, especially those of the granular series.

A normal **balance between these two processes** is maintained in health; whilst, in disease, there is a latent capacity for the increased production of any or all of the blood-cells to meet the increased demand for them, whether this be due to the necessity of replacing cells destroyed by the disease, as in the anæmias, or to the fact that more blood-cells are required to combat the attack of the invading bacterial or other pathogenetic agent, as is seen in the various inflammatory and suppurative conditions— the fatty marrow forming an important potential additional area for the production of this reaction in the marrow.

(2) **Blood-Destruction, Phagocytosis, etc.**

The marrow, like the liver and spleen, constitutes a very important **hæmolytic** area, and this function is greatly increased in most of the acute and chronic toxic diseases, e. g. the acute infective fevers, septicæmias, malaria, etc.; the anæmias, especially the pernicious forms; and the "cachexias," especially malignant disease, etc. (See Plates III, fig. 2, and XIV, fig. 4.)

Phagocytosis of pathogenetic organisms also occurs to a considerable degree in many diseases, the marrow appearing to be specially liable to the presence of micro-organisms; and, as in the case of the spleen in many diseases, pure cultures of these may frequently be obtained from this tissue, e. g. in pneumonias, streptococcal and other septicæmias, etc. Some blood- and other parasites pass certain stages of their development in the bone-marrow, and endothelial and other forms of phagocytic cells may be found containing englobed parasites or their remains, e. g. in malaria, trypanosomiasis, etc.

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[1] Carnegie Dickson, *loc. cit.,* p. 62.

(3) **Formation, Nutrition, and Absorption of Bone.**—These functions are of great importance, but, for the details of such processes, reference must be made to special physiological works upon this subject. Under certain pathological conditions, very rapid **absorption of bone** may occur, e. g. in the enlargement of the medullary cavity, to allow of greater scope for the proliferation and expansion of the contained marrow, a process which may, in some cases, take place with great rapidity. The probability that many conditions which have previously been regarded as primary diseases of bone, e. g. osteomalacia, " osteoporosis," osteitis deformans, and analogous conditions, may, upon further investigation, be found to come under this category, must be borne in mind; whilst a somewhat similar absorption of bone is seen in pernicious anæmia.

(4) **Functions in Relation to General Nutrition and Especially with regard to Metabolism of Fat.**—Fatty or yellow marrow is very richly supplied with blood-vessels; and, in fevers, etc., the fat may be very rapidly absorbed from the tissue, which thus acts as a store-house for this substance. It is also possible that the red marrow, like many of the other glandular organs in the body, may give rise to an internal secretion of importance to general nutrition and metabolism; but, owing to the impossibility of experimentally eliminating the action of the tissue on account of its wide anatomical distribution, it is as yet difficult to prove the truth of this supposition.

LEUCOCYTOSIS

A well-marked increase in the number of leucocytes is—except in the case of certain so-called " blood-diseases " such as the leucocythæmias —termed a **leucocytosis.** The normal number of white cells in the peripheral blood is about 8,000 per cubic millimetre. A definite increase, say up to 11,000 or 12,000, occurs in some physiological, and in many pathological, conditions, and, in the latter, a count of 15,000, 20,000, or 25,000 per c.mm. may also frequently be obtained; whilst, in exceptional circumstances, it may rise even to 60,000 or 70,000, or more. Many modern writers are inclined to regard even the leucocythæmias as merely very excessive and perverted forms of leucocytosis due to some unknown toxic agent—though others regard them as analogous to, or even actually, a diffuse neoplastic change in the blood-forming organs and tissues.

CLINICAL VARIETIES OF LEUCOCYTOSIS.—These may be divided into those which are respectively **physiological, experimental and therapeutic,** and **pathological.** In the first of these categories comes the **leucocytosis of digestion,** which does not usually exceed about 15,000 white cells per c.mm., the lymphocytes being specially increased : the **leucocytosis of the new-born infant,** which may be from 14,000 to 20,000 or more : the **leucocytosis of pregnancy** (11,000 to 13,000), and **that following parturition** (10,000 to 12,000) : and the **leucocytoses following violent exercise, the use of cold baths, etc.**

Certain experimental and therapeutic measures may lead to the production of leucocytosis: for example, the exhibition of drugs and chemicals such as the salicylates, potassium chlorate, phenacetin, or the inhalation of chloroform. Similarly, a considerable increase of leucocytes may occur after the administration of certain animal extracts, etc., for example of the thyroid gland and bone-marrow, and more especially after the use of nucleic acid, a substance which has been employed for the artificial production of leucocytosis. In surgical practice, a post-operative rise is very frequently observed, even in aseptic cases. The leucocytosis produced by therapeutic inoculation with certain bacterial cultures and toxins is identical in its nature with the same conditions produced by disease, and, therefore, calls for no further comment here. In a series of cases of streptococcal infections (in three of which the streptococci were obtained by blood-culture), which were characterised by leucopenia in place of the usual leucocytosis, Carnegie Dickson has observed that a therapeutic leucocytosis may be rapidly stimulated artificially by the intravenous injection of horse-serum, usually accompanied by a corresponding improvement in the patient's condition.

LEUCOCYTOSIS PRODUCED BY DISEASE.—The most important variety of leucocytosis due to this cause is that seen in the majority of inflammatory and toxic diseases. An increase of the white cells—more especially of the polymorphonuclear cells—occurs in most of the acute infective diseases, notably in pneumonia, acute rheumatism, and diphtheria. Exceptions to this general rule are found in the case of typhoid fever, influenza, measles, and also in tuberculosis; and, if a polymorphonuclear leucocytosis is discovered in patients suffering from these diseases, the presence of some complication such as pneumonia, suppuration, or other inflammatory condition, is to be suspected.

Inflammatory and toxic leucocytosis is found, not only when the disease is a general one, but also when the lesion is localised, for example, in local inflammatory and suppurative conditions such as abscess, appendicitis, etc., and its occurrence is of great value in the diagnosis of these conditions.

A rise in the leucocyte-count may also occur in certain parasitic—and probably at the same time toxic—diseases. In these, the increase may specially affect varieties of white cell other than the common or polymorphonuclear leucocytes. Thus, in many parasitic intestinal and skin diseases, there may be a marked rise in the eosinophil cells; in malaria, the large hyaline mononuclear cells are increased—and so on.

Leucocytosis may also occur in poisoning with coal-gas, quinine, chronic lead-poisoning, etc.; whilst the increase observed in cases of ptomaine-poisoning is analogous to the condition produced by infective bacterial and other organismal toxins—the ptomaines being produced outside the body by bacterial decomposition in food, etc.

Post-hæmorrhagic Leucocytosis is a well-recognised phenomenon. Loss of blood stimulates the general hæmopoietic activities of the bone-

marrow, and leads, at first, to increased production both of red and of white cells, i. e. both types of blood-cells produced by the tissue. Later, the marrow adjusts its output to the particular circumstances of the case; and the special type of change required—in this instance mainly an erythroblastic one—is established, in order to replace the red cells lost by the hæmorrhage.

The term "**cachectic leucocytosis**" is not a very fortunate one. It implies that a rise in the leucocyte-count is found in many chronic wasting diseases; but these do not form a very definite group, and, in many such cases, the leucocytosis is probably due to some superadded chronic toxæmia, or to local inflammatory processes, etc. Leucocytosis is described by many authorities as occurring in cases of malignant disease in general, but it is **not** a constant phenomenon in these (see p. 623), and, when present, is usually rather to be regarded as an indication of some secondary phenomenon such as necrosis, ulceration, and bacterial infection. In many so-called cachectic diseases, the occurrence of leucocytosis is rare, or it does not take place at all, for example, in tertiary syphilis, tuberculosis, chronic nephritis, etc. Any marked increase of leucocytes in such cases suggests the presence of some such complication as local inflammation, suppuration, necrosis, or hæmorrhage.

Terminal or Ante-mortem Leucocytosis.—Sometimes, a very marked increase of white cells in the peripheral circulation occurs in patients who are moribund. In some instances, this may be due to the presence of terminal bacterial infection; but a remarkable tendency of the polymorphonuclear cells to leave the marrow at or just before death has been observed by several writers, and no doubt accounts for the increase, in many cases, of these cells in the blood at this period.

CYTOLOGICAL TYPES OF LEUCOCYTOSIS :—

1. **NEUTROPHIL, POLYMORPHONUCLEAR or COMMON LEUCO-CYTOSIS** (see Plate XIV, fig. 2).—In the great majority of inflammatory and allied diseases, it is especially the cells of the finely-granular neutrophil series that are increased. The cells of this series found in the blood in such cases may not be, and, in fact, most commonly are not, entirely confined to the adult or fully-developed polymorphonuclear members of the neutrophil group—though, as a rule, these cells specially predominate. The immature intermediate cells of the series, and even the parent-myelocytes themselves, may occur in considerable numbers; and the condition present is, therefore, most accurately described as a **neutrophil leucocytosis.** The number of these cells, and also their degree of development or maturity, depend upon various factors, more especially upon the nature, quality, intensity, and duration of application of the causal irritant, and also upon the age and vitality of the patient, and the healthy condition or otherwise of the hæmopoietic tissue of the bone-marrow. It is largely upon these phenomena that the so-called **Arneth-Count** is based, particular attention having been directed by Arneth to the enum-

eration of the number of lobes in, and other characters of, the nuclei of the polymorphs. These lobes are reduced in number in the more immature cells of the series, and *vice-versa* (*see* also p. 577).

Certain irritants appear to have the capacity of **attracting** leucocytes towards them, this phenomenon being termed **positive chemiotaxis;** whilst others do not possess this power. (*See* also under **Immunity,** p. 746.) In positive chemiotaxis, the leucocytes are attracted towards the seat of irritation, and may pass from the vessels in large numbers. In order to meet the increased demand for such cells, greater numbers pass from the marrow into the blood; and, if the demand be sufficient in intensity and duration, the blood-forming tissue of the marrow proliferates to supply it, as has already been described on p. 593. It has also been noted that the occurrence of this leucoblastic reaction of the bone-marrow may be prevented by previous degeneration or exhaustion of the tissue by such conditions as syphilis, alcoholism, etc. In these cases—the capacity for responding to the increased call being diminished or lost—the supply of leucocytes may be even less than normal. Absence of any increase is termed **aleucocytosis;** whilst an actual diminution in the normal leuco-cyte-count is known as **hypoleucocytosis,** or **leucopenia**—these conditions being not infrequently seen in pneumonia occurring in alcoholic subjects —**pneumonia with leucopenia,** a very serious disease which usually leads to a rapidly fatal issue (*see also* pp. 594 and 603): or in profound infections.

Where the demand is moderate and the patient has been previously in good health, the leucocyte-count may number, say, 10,000, 12,000, or 14,000. A more serious call, especially if the patient's resistance is some-what lowered, may lead to an increase to 18,000 or 20,000; whilst in severe cases, say of appendicitis or of pneumonia, the count may be. 25,000, 30,000, or 40,000. In cases where the resistance has been lowered by previous disease or other cause, the leucocytes may reach the number of 60,000 or 70,000, or even more. Thus, in the most serious cases—those of severe disease in debilitated subjects—the reaction may either be deficient or absent, or it may be excessive in amount.[1]

In the **milder forms of leucocytosis,** the increase is almost entirely one involving the **mature** or **fully-developed polymorphonuclear neutrophil cells,** though a certain number of slightly immature forms are found. When the call is **more severe,** many **immature** polymorphs, and perhaps some **intermediate myelocytes** with horseshoe-shaped nuclei, appear in the blood; whilst **in very severe cases,** *e. g.* of pneumonia, it is by no means uncommon to find a number of **neutrophil myelocytes**—sometimes as many as 10 per cent. or more, at or near the crisis in this disease. **Large numbers of myelocytes** are found in the blood of **smallpox** cases; and in **serious or fatal cases of diphtheria in children,** the occurrence of as many as 16 per cent. has been recorded. The presence of neutrophil myelocytes

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[1] NOTE.—In acute lobar pneumonia, prognosis is usually bad with a leucocytosis of under 10,000; the mortality is least when the count is between 20,000 and 30,000; and again higher between 30,000 and 60,000 and upwards—though recoveries have been reported with even 95,000 and 105,000 leucocytes per c.mm.

is also described in many of the **anæmias,** both primary and secondary, and in some cases of **uræmia, acute mania, diabetic coma, exophthalmic goître,** etc. (*See* also pp. 577 and 600.)

2. **LYMPHOCYTOSIS,** or relative increase of the lymphocytes, occurs very readily **in infancy and in childhood,** the lymphoid tissue being specially active during the earlier periods of life. An increase in the number of lymphocytes is usually present in **whooping-cough, rickets,** and **congenital syphilis;** and may also be found in **tuberculosis,** in which condition, however, it is not constant, nor does the number of such cells in the blood appear to have any particular relation to the number of so-called lymphocytes in the exudates, *e. g.* in pleuritic effusion, in this disease. The subject of the increase of lymphocytes or lymphocyte-like cells in leukæmia and in some sarcomatous tumours of lymphatic glands is dealt with in the sections on these diseases (pp. 610 and 611).

3. **LARGE MONOCYTOSIS, or INCREASE OF LARGE HYALINE MONONUCLEAR CELLS.**—These may be relatively increased in numbers in some diseases, notably in malaria, in which they are specially concerned in the phagocytosis of the parasites, and are frequently observed to contain pigment derived from these (*see* Plate XIV, fig. 1). An increase of these cells has also been noted in cases of sympathetic optic neuritis.

4. **EOSINOPHILIA.**—As a general rule, the number of eosinophils in the circulating blood is diminished in most inflammatory and septicæmic diseases. Thus, in pneumonia, they are either extremely scanty, or they may entirely disappear during the course of the fever, their reappearance at or after the crisis being usually regarded as a favourable phenomenon. In certain diseases, however, **eosinophilia** or an increase of these cells may occur, either **relatively,** or **as part of a general increase** in the number of white cells. Apart from **myelogenous leukæmia,** in which a marked degree of relative eosinophilia occurs, these cells may be very greatly increased in certain **parasitic** diseases, for example in **trichinosis,** and infection with some **intestinal worms,** such as *Ankylostoma,* some of the tapeworms, *Oxyuris, Ascaris lumbricoides,* and others. Eosinophilia is also seen, sometimes to a remarkable degree, in many **skin-diseases,** *e. g.* pemphigus, eczema, scleroderma, psoriasis, urticaria, etc., and in syphilitic cases exhibiting special skin-lesions. A peculiar exception to the general rule that the eosinophil leucocytes tend to be diminished in numbers during febrile leucocytosis is seen in the case of scarlet fever, perhaps from the extensive implication of the skin in this disease. In some lung-diseases, notably in **bronchial asthma,** these cells may be considerably increased in the blood, and are also found in large numbers in the sputum. The occurrence of eosinophils in various exudates is described in the Chapter on **Inflammation** (pp. 176 to 179), and, in this connection, it is noteworthy that such local infiltrations with eosinophils, sometimes "massive" in degree, may be associated with their diminution in, or perhaps even complete disappearance from, the peripheral blood.

No very definite ratio between the number of the eosinophils in the blood and in the bone-marrow—in which tissue they are, in part at all events, produced—has as yet been made out. Thus, in some cases of pneumonia, where they have entirely disappeared from the circulating blood, they may be diminished, unchanged, or even increased in number in the marrow.[1]

5. **INCREASE OF MAST-CELLS.**—The significance of these cells is not yet known. The only condition in which they are specially increased is **myelogenous leukæmia.** Slight increase in their numbers from time to time in the blood, in a series of cases of **acromegaly,** has been observed by one of the authors.

MIXED LEUCOCYTOSIS.—In many cases, **several** varieties of cells may be found in increased numbers in the blood.

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NOTE ON ALEUCOCYTOSIS AND LEUCOPENIA

(See also pp. 594 and 601.)

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Diminution in the numbers of white cells—more particularly the polymorphs, but also the lymphocytes—may be seen as a **transitory phenomenon preceding the establishment of leucocytosis** in many of the acute diseases. This may be due to two different sets of causes : (1) the cells may be partially withdrawn from the peripheral circulation, and thus not be found in their usual numbers in the drop of blood examined, an accumulation taking place in some of the internal organs—especially in the capillaries of the lung—or in some of the other tissues of the body ; [2] or (2) there may be defective formation, and hence defective replacement, of those in the circulation. In the latter case, this deficient reaction may persist, if the infection is specially virulent, or, as has been said above, if the patient is enfeebled and his blood-forming tissues, especially the bone-marrow, be exhausted, as for example in alcoholic or in syphilitic subjects, or in old persons—these cases usually having a fatal termination. The absence, without any very obvious cause, of leucocytosis in certain streptococcal cases—although an inflammatory leucocytosis is the general rule in streptococcal infections—has already been noted above (p. 599), together with the observation that a marked leuco-cytosis can usually be rapidly established in such cases by the intravenous administration of horse-serum. Mention has already been made, of certain acute infective diseases in which leucocytosis does not occur, viz. **acute miliary and other uncomplicated forms of tuber-culosis, typhoid fever, influenza,** and **measles.** Diminution in the number of white cells occurs in some cases of **starvation** and **malnutrition,** *e. g.* in cancerous stricture of the œsophagus; and also in **pernicious anæmia,** in **splenic anæmia,** and in **some severe secondary anæmias,** *e. g.* those resulting from rickets, syphilis, hæmorrhage, etc.

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[1] Carnegie Dickson, *loc. cit.,* Appendix II.   [2] See footnote, pp. 576–7.

SPECIAL PATHOLOGY OF THE BLOOD AND BLOOD-FORMING ORGANS

Some of the more important **pathological alterations in the blood** now fall to be described. Many of these are recognised to be the results of certain reactions on the part of the hæmopoietic or blood-forming tissues, produced by the action of various toxic substances of known or unknown origin—for example, the toxins of bacteria, animal parasites, etc., and also, it is supposed, certain poisons generated by perverted metabolic processes within the tissues and organs of the patient himself. In any given instance, two sets of processes must be considered. Firstly, what may be regarded as the **physiological reaction of the blood-forming tissues,** in order to combat, and, if possible, to neutralise, the effects of disease. Secondly, the **pathological or harmful effects upon the hæmopoietic tissues of the poison or irritant, producing aberrations,** it may be, **in the functions of these tissues,** varying in nature and in degree, or perhaps even causing their wide-spread destruction. Thus, **the anæmias** are conditions in which the erythroblastic functions of the marrow are overstrained or not fully developed, imperfect, or inadequate to meet the demands made upon this tissue by the excessive and increasing blood-destruction. In some cases, as in pernicious anæmia, the hæmopoietic functions of the marrow are also **perverted.** In the **leucocythæmias** or **leukæmias,** there is some factor, of unknown nature, which stimulates the blood-forming tissues, especially the marrow, to produce enormous numbers of immature or otherwise aberrant white cells. Thus, in the consideration of any of the so-called "primary diseases of the blood," it is always possible to refer the abnormal phenomena found to some **antecedent pathological process in the hæmopoietic tissues.** Where a definite cause of this antecedent process has been discovered, e. g. the presence of some parasitic or bacterial infection, neoplasm, etc., the blood-condition is usually spoken of as **secondary;** whilst, if no such cause has yet been discovered, the disease is sometimes classified as a **primary** disease of the blood and blood-forming tissues. In this connection it is, of course, obvious that, as our knowledge increases, all such morbid conditions of the blood will in time be proved to be " **secondary,**" i. e. due to some definite ascertainable cause. After this preliminary note, the detailed consideration of these so-called primary and secondary conditions of the blood may be discussed.

LEUCOCYTHÆMIA OR LEUKÆMIA

Leucocythæmia or leukæmia is a disease, or rather a group of diseases, of unknown origin, characterised by an increase—often to an enormous degree—of the leucocytes in the blood, and usually shewing aberrant or abnormal types of blood-cell: characterised also by certain clinical symptoms such as progressive weakness, wasting, hæmorrhages from the nasal and other mucous membranes, etc.: and by well-marked pathological changes in certain organs and tissues.

The disease was described by Hughes Bennett, in 1841, as "**leucocythæmia**" or "a condition of the blood resembling suppuration," this "pyoid" condition of the blood being accompanied by enlargement of the liver and spleen. A few weeks later in the same year, Virchow described a case of what he called "**weisses Blut**" or "**Leukæmia**," and he distinguished clearly between this condition and true pyæmia, emphasising the presence of the characteristic pathological changes in the hæmopoietic tissues. Later, Virchow divided the cases into **splenic** and **lymphatic varieties**, the bone-marrow at that time not having been yet recognised as a leucocyte-producing tissue. In 1879 and 1880, Ehrlich's discoveries in connection with the bone-marrow and the types of blood-cells originating in it, led to the classification of these diseases into :—

(a) **Spleno-Medullary** or **Myelogenous Leukæmia (Myelocythæmia).**

(b) **Lymphatic Leukæmia** or **Lymphocythæmia.**

An enormous amount of research has since been carried out in connection with these diseases, and **all intermediate gradations between these two main types** have been observed, as well as certain **atypical forms**—amongst them cases which appear to be more or less intermediate between the leukæmias and such diseases as Chloroma and Sarcoma, as well as leukæmias in which the usual blood-picture is absent (Pseudo-Leukæmia —the so-called "Leukämie ohne Leukämie" of some German writers). We shall content ourselves with the description of the two main recognised types mentioned above.

1. SPLENO-MEDULLARY OR MYELOGENOUS LEUKÆMIA, OR MYELOCYTHÆMIA

This variety is said to be commoner than the lymphatic form, and usually lasts from two to five years, though more acute cases occasionally occur.

The **ætiology** of the disease is still quite unknown. Age, sex, and heredity appear to have an undoubted influence on its occurrence, the condition being distinctly commoner in males, especially during middle age. Pregnancy, trauma, influenza, syphilis, tuberculosis, malaria, rickets, and many other conditions have, in individual cases, been alleged as predisposing causes; whilst some authorities, with considerable justification, regard the disease as a reaction of the blood-forming organs, produced by some infective or toxic agent of unknown nature. Many,

however, still hold that it is a " primary " disease of the hæmopoietic organs and tissues—possibly neoplastic in nature.

Pathological Changes in the Blood.—The **colour** of the blood may be little altered in the less extreme cases, or it may be distinctly paler than normal. It may be **more watery** in consistence, owing to the associated anæmia, and **coagulation** is usually delayed—sometimes greatly so. The **alkalinity** of the blood may be diminished; and the occurrence, after death, of " Charcot-Leyden " octahedral crystals is described.

The white cells are enormously increased in numbers, e. g. from 100,000, 150,000, or 200,000 in cases of moderate degree, up to 500,000 or even 650,000 or more in severer cases.[1] The numbers usually vary considerably from time to time during the course of the disease, and even at different periods of the day, **temporary remissions** and **relapses** being of frequent occurrence. A fall in the leucocyte-count is often observed just before death, and a similar fall may occur from the supervention of some intercurrent acute disease, such as pneumonia. The varieties of white cells specially increased are those of the **granular series,** i. e. (i) the polymorphonuclear neutrophil leucocytes, the marrow-cells from which they are derived, and the cells intermediate between them in development, (ii) the coarsely-granular eosinophil cells, and (iii) the mast-cells. Lymphocyte-like cells may also be increased in absolute, but usually not in relative, numbers. (See Plate XIV, fig. 3.)

The relative numbers of the **adult** and of the **immature members of the neutrophil series** vary considerably in different cases, and also during the course of the disease in individual patients, both treated and untreated. All forms, from the non-granular myeloblasts or pre-myelocytes, and the large granular myelocyte of Cornil—through the intermediate myelocytes and immature polymorph cells—down to the fully developed or adult polymorphonuclear leucocyte, are found. The earlier members of the series—the myelocytes—average 35 per cent. of the leucocytes present, though in some cases they may be more numerous. They may number as many as 100,000 or more per c.mm., and, as they increase, the poly - morphs—usually about 50 per cent. of the total leucocytes present—may correspondingly diminish in numbers. One of the most notable features of myelocythæmic blood is the large number of **eosinophil cells** which are often present, e. g. 5 or 10 per cent. being quite a usual number. A considerable proportion of them may be eosinophil myelocytes, characterised by their larger size and single rounded nucleus. These latter, however, are never so numerous as the neutrophil myelocytes. The increase in **mast-cells** is a very constant phenomenon, and is more marked in this disease than in any other known condition—counts of 30, and even 40, per cent. having been recorded in some cases. It will be noted that these figures, being percentages of what is often a very large total leucocyte-count, represent very considerable absolute numbers for the individual types of cells mentioned.

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[1] It must be borne in mind that the figures given are for blood drawn from the *peripheral* circulation only.

The **red corpuscles,** at first often not seriously affected, become progressively decreased in numbers as the disease advances. This decrease may, however, be comparatively slight in cases of moderate severity, *e. g.* to 3,000,000, or in severer cases perhaps to 2,000,000 per c.mm. In fatal cases, the number may be even under 1,000,000. The **hæmoglobin** is diminished in proportion. **Nucleated red cells** are frequently seen in considerable numbers, and are mainly **normoblasts.** In the later stages and in severe cases, alterations in shape (**poikilocytosis**) and size (**anisocytosis**), and various **degenerative** phenomena such as fragmentation of the nucleus, may be observed.

Blood-plates are often increased in number.

Changes in the Organs and Tissues :—

Bone-Marrow.—The change in the bone-marrow is essentially a **leucoblastic reaction,** with increased production of the granular series of white cells, neutrophil, eosinophil, and basophil. The activity of the red marrow is enormously increased, and the fatty marrow is completely transformed into actively hæmopoietic tissue. To the naked eye, the marrow, owing to the enormous numbers of white cells present, usually shews a thick fluid, pale, homogeneous, creamy appearance, very much resembling pus—the so-called " pyoid " or " puriform " marrow, the colour varying—usually yellowish, sometimes pinkish-yellow, and occasionally greenish-yellow. In old-standing cases, especially in elderly patients, **atrophic** and **degenerative changes** tend to supervene, the active marrow becoming transformed into inert, translucent, gelatinous material, which may be pale yellow to dark red in colour, or may, in some cases, present a patchy mixture of these. **On microscopical examination,** the marrow from a typical case of myelogenous leukæmia shews an enormous increase in neutrophil myelocytes especially, but also in eosinophils and mast-cells. In freshly prepared films, evidence of this active proliferation is also shewn by the presence of very numerous mitotic figures in these cells. Along with this enormous increase in granular white cells, a corresponding decrease or atrophy occurs in the erythroblastic elements, some of which may pass into the blood-stream while still nucleated. Large blood-destructive or hæmolytic **phagocytic cells** are usually present in large numbers. The fat-cells are greatly diminished, and may have even entirely disappeared. The **megakaryocytes,** or giant-cells, though often smaller in size than normal, are frequently increased in number.

Spleen.—This organ is almost invariably enlarged—as a rule, greatly so, especially in the more chronic cases. It usually maintains a comparatively normal shape, the notches being very distinct. It may weigh from five to eight or even, in some cases, over eighteen pounds; and it may measure eight or ten up to over twenty inches in length, its lower extremity (unless anchored by previous adhesions or by an abnormally developed costo-colic fold of peritoneum, in which case the enlargement may take place upward), usually passing downwards and to the right, and often coming to lie in the right iliac fossa. The **capsule may be**

thickened, usually irregularly, from recurrent attacks of perisplenitis; and there are, frequently, adhesions to surrounding structures. The spleen is firm and hard, and usually presents on its surface a number of large, yellowish-white, homogeneous, necrotic areas of **infarction,** most probably produced by thrombosis. Old infarcts, undergoing partial or complete absorption, may be present. **On section,** the spleen-tissue—unless softened by terminal septic infection—is smooth, and somewhat dry and firm, its colour varying in different cases, but being most commonly of a homogeneous pinkish or pale red tint; and the Malpighian bodies are obscured and cannot usually be distinguished. **Microscopically,** the changes in the enlarged spleen vary considerably in different cases and at different stages of the disease. In the early stages, there is
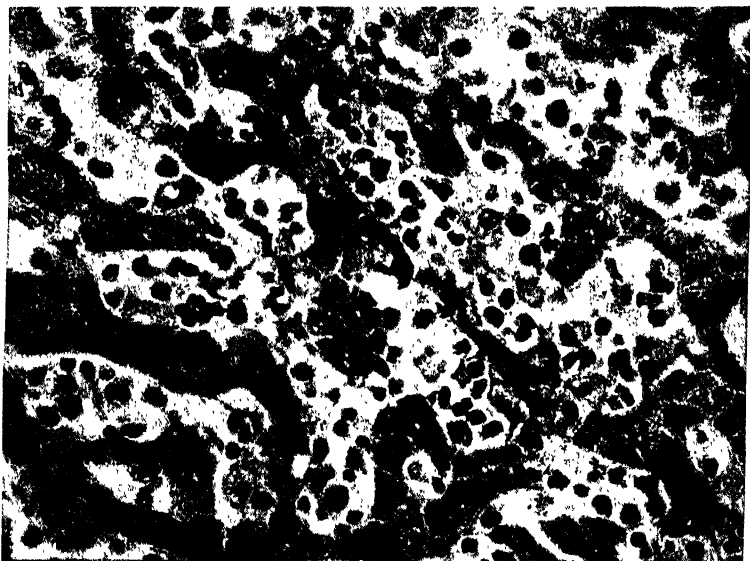
Fig. 281.—*Liver in Myelocythæmia.* Large numbers of cells, chiefly myelocytes, an between the columns of liver-cells—mostly within the capillaries. × 400.

marked **cellular increase**; whilst later, various **degenerative processes,** especially **fibrous overgrowth of the adenoid reticulum,** supervene, both in the Malpighian bodies and in the pulp. In the latter, there are, usually, marked **proliferation and phagocytic activity on the part of the endothelial cells lining the sinuses.** Some of these cells may attain large dimensions, and frequently shew marked increase in their normal functions of destroying effete red blood-corpuscles, as well as members of the abnormally increased leucocyte-series. The pulp and its sinuses sometimes contain nucleated red cells in excess of those present in the circulating blood. There is no evidence that this excess is due to any local formation of these cells, and it is much more likely that they have been sifted or filtered out from the blood as abnormal, preparatory to their destruction by the phagocytic cells. It is probable that the myelocytes, also seen

in considerable numbers, are similarly in process of destruction. In the spleen, there are thus hyperplasia and increased activity of its pulp-cells, an accumulation and destruction of the abnormal blood-cells, and a progressive atrophy and fibrosis of its component tissues. The conditions in this organ are, therefore, to be regarded as **effects,** rather than as a cause, of the disease, the organ acting as a filter and destroyer of the abnormal blood-cells. Under X-ray treatment, temporary diminution in the size of the organ may be produced.

Liver.—This organ is usually considerably increased in size, but not, as a general rule, to such an extent as in lymphocythæmia. It is pale in colour, the capillaries between the columns of liver-cells, and also the connective-tissue framework, e. g. of the portal tracts, being crowded with granular myelocytes and polymorphs, many of the latter being very immature. These are said by some to be an " infiltration " or mechanical lodgment of increasing numbers of such cells from the blood; but other and more recent observers believe that actual proliferation by mitotic division occurs in situ, and that the condition is a return to the hæmopoietic activity exhibited by the liver during fœtal life. Occasionally, localised tumour-like nodules of such cells may occur.

Lymphatic Glands.—These do not, as a rule, exhibit any general enlargement in this variety of leukæmia, though such enlargement may be seen in some of the so-called "intermediate" cases. The glands usually shew a certain degree of hyperplasia, more especially of the **phagocytic endothelial cells** lining the lymph-sinuses.

Kidneys.—These organs are generally somewhat enlarged, pale, and often fatty. **Microscopically,** their capillaries and connective-tissue framework, e. g. between the tubules, are crowded with myelocytes. Similar accumulation of these cells may also be seen in the capillaries of the **lungs, heart-muscle,** and elsewhere.

Hæmorrhages, especially from mucous membranes, frequently occur. Death may result, in such cases, from large **cerebral hæmorrhages** or from **hæmorrhage into the lungs;** though extravasation of blood into other internal organs is not so common as in lymphocythæmia.

2. LYMPHATIC LEUKÆMIA OR LYMPHOCYTHÆMIA

This is said to be less common than the myelogenous form, in the proportion of one to ten, but, since the recognition of the occurrence of an **acute type** of the disease, larger numbers of cases of lymphocythæmia have been reported, and the disease, especially in its acuter forms, is by no means very rare in adolescents, children, and infants. Under the general term **lymphatic leukæmia,** it is probable that several closely allied conditions are at present described; and, as already mentioned, certain cases appear to be **intermediate in type** and to form a link between the two main forms of the disease—myelogenous and lymphatic. Further, in each of these, but especially in the case of **lymphocythæmia, there are**

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acute and **chronic varieties,** varying in their duration from a few weeks up to several years.

Blood. —There is an enormous **increase of " lymphocytes," or lympho-cyte-like cells,** whose characters are indistinguishable from those of the lymphocytes of normal blood (*see* Plate XIV, fig. 4). The cells are usually of the **small** variety, and these may constitute some eighty or ninety per cent. of the total leucocyte-count. They are, however, sometimes **of larger size,** *e. g.* from 10 to 15 μ in diameter; and these cells may; in rare cases, predominate, especially in some of the more acute forms of the disease. The total number of lymphocytes does not usually exceed about 100,000, though, occasionally, much higher numbers may be met with. Except in certain intermediate cases above referred to, there is, usually, no cor-responding increase of polymorphonuclear cells and myelocytes, either neutrophil or eosinophil, or of mast-cells, which may be, and usually are, diminished in numbers.

Erythrocytes.—The red corpuscles are affected in much the same way as in myelocythæmia, except that nucleated forms are usually few in number, or even absent, until, at all events, comparatively late in the course of the disease. They may, as in any profound anæmia, begin to appear when the erythrocytes have become reduced to less than half their normal number.

Blood-Platelets tend to be diminished in numbers in this variety of leukæmia, rather than increased as in myelocythæmia.

The **Bone-Marrow** usually shews great " infiltration " with lympho-cyte-like cells, and a corresponding diminution or even, in large areas, a disappearance of the other elements normally present. This form of leucoblastic change is often extremely **irregular in its distribution,** giving a characteristic patchy red-and-white appearance to the marrow on section. **Degenerative changes** may supervene later. As to the **nature of these lymphocyte-like cells,** opinion varies greatly. Some regard them as an infiltration of the tissue by cells produced elsewhere, *e. g.* in the lymphatic glands; but opponents of this theory point out that the marrow is often extensively affected in cases where these glands shew little or no change. Lately, the view, with which we are strongly inclined to agree, that these cells are, in reality, **earlier members of the myelocyte series,** has gained ground, and it is believed that the lymphocyte-like cells, especially the larger varieties, are simply **non-granular pre-myelocytes or myeloblasts,** *i. e.* myelocytes in which the granules have not yet developed. In some cases of myelocythæmia, many of the myelocytes may be extremely poor in granules, and some may have none distinguishable, in which case the cell closely resembles the " large lymphocyte " of lymphocythæmia. **Megakaryocytes** tend to be diminished in numbers.

Spleen.—This organ is not so profoundly affected as in myelogenous leukæmia. If enlarged, it is usually only moderately so. Its pulp is

crowded with the lymphocyte-like cells, and, in some cases, the Malpighian bodies are enlarged and hyperplastic, sometimes in marked degree.

Lymphatic Glands.—In certain cases, there may be wide-spread enlargement supervening early in the course of the disease, or the enlargement may affect only one or more groups of glands, e.g. the cervical, the axillary, the inguinal, the prevertebral, or the mesenteric; and, in several cases observed by one of us, the glands at the hilus of the liver have been specially affected. More commonly, two or more of these groups are involved. In other cases, the glandular enlargement is not a marked feature of the disease. Occasionally, the lymphatic enlargement is local only, and may resemble, say, a mediastinal tumour of the nature
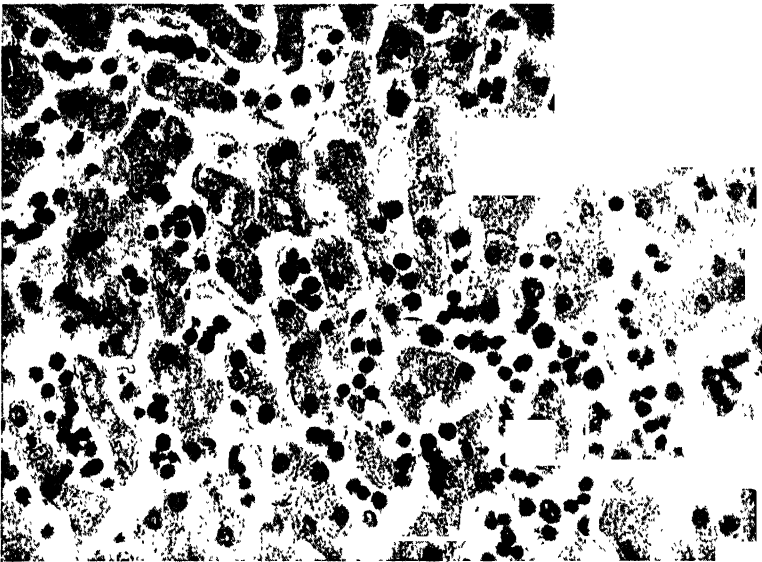
FIG. 282.—*Liver in Lymphocythœmia.* Shewing the infiltration with small "Lymphocytes." × 400.

of a lymphosarcoma. This variability in the pathological condition of the lymphatic glands suggests the probability that a group of allied diseases is in reality being dealt with, in some of which the condition is, apparently, **primary in lymphadenoid tissue :** in others, **in the bone-marrow:** whilst, in a third variety, **both of these structures** may be affected.

The **Liver** and the **Kidneys** are often very markedly enlarged—much more so than in the myelogenous type—there being, sometimes, an enormous " infiltration " of the tissues with lymphocytes, or even the appearance of irregular nodules and masses of adenoid tissue resembling tumour-growth. Such organs may exhibit a uniform dead-white appearance, but often white lines of " infiltration " may be seen along the blood-vessels and in the connective-tissue framework. Other organs, e.g. the **heart** and **lungs,** may also shew similar changes.

Multiple Hæmorrhages may occur. They are, as a rule, not, so profuse as in the myelogenous type. They are often widely scattered, and may be found, for example, in the skin, kidney, enlarged lymphatic glands, etc. In some cases, they may be absent.

When the anæmia becomes pronounced, fatty change, in varying degree, is found in the organs.

These **leucocythæmic diseases,** therefore, bear a resemblance, on the one hand, to **infective conditions** producing excessive and aberrant types of leucocytosis, and, on the other, to **diffuse tumour-like conditions** affecting the hæmopoietic and other tissues and organs. The ultimate nature of their causation is as yet quite unknown.

POLYCYTHÆMIA RUBRA, CYANOSIS, ERYTHRÆMIA, ETC.

The **Red Blood-Corpuscles** may be **increased in number** in a variety of conditions. Apart from the temporary concentration of the blood in severe diarrhœa, etc., such increase may be in order to meet an extra demand for oxygen-carrying capacity on the part of the blood, as, for example, at **high altitudes,** at which the atmosphere is rarer and its oxygen-content therefore less per unit of bulk. All vertebrates, man included, living on high mountain-ranges or plateaux, possess a number of red corpuscles in excess of the normal, and a temporary visit to high altitudes, or even, it is said, an ascent in an aeroplane or air-ship, may give rise to a transitory increase.

Polycythæmia and Cyanosis may also result from the respiratory embarrassment of **heart- and lung-diseases,** and is often well marked in certain cases of congenital heart-disease, such as patency of the foramen ovale, ductus arteriosus, etc. In such cases of **Congenital Cyanosis,** the red corpuscles may be eight, ten, or even twelve or more million per c.mm. Lesser degrees of polycythæmia may be found in mitral stenosis and other forms of acquired heart-disease.

In addition to the above forms, another variety of polycythæmia, of unknown origin, is now recognised. This has been variously termed **Erythræmia, Splenomegalic Polycythæmia, Erythrocytosis Megalosplenica, Vaquez's Disease, Osler's Disease,** etc., the first of these names, applied to it by Osler, who has called special attention to the condition, being perhaps the most suitable. The disease begins usually in middle life, being of slow onset and affecting both sexes equally. The **red corpuscles** may number eight, ten, or even over thirteen million, the average being ten million, per c.mm., and the **hæmoglobin** 115 to 160 or even 200 per cent., though the **colour-index** is usually *below* unity. The total number of **leucocytes** may, or may not, be increased—in about half the recorded cases it was over 20,000 c.mm.—but the polymorphonuclear cells are usually *relatively* increased and may constitute 80 per cent. or more of the whole, the **lymphocytes** being proportionately reduced in their percentage.

Myelocytes and nucleated reds occasionally appear, and the **blood-platelets,** as a rule, shew an abnormally high count. The **total volume** of the blood is increased.

The **bone-marrow** shews a profound erythroblastic change, and the **spleen** is usually (though not invariably) greatly enlarged, and may shew infarcts. The **visceral blood-vessels,** especially those of the **liver,** are usually much engorged.

The cause of the disease is unknown, but the condition appears to be somewhat analogous to the leucocythæmias, the reaction of the marrow being here **erythroblastic** instead of leucoblastic. The enlargement of the spleen is due probably to its efforts to cope with the destruction of the abnormally numerous red cells in the blood—analogous to the leucocyte-destruction in the leucocythæmias. (*See also* p. 660.)

" **Enterogenous Cyanosis** " has already been considered (p. 575).

ANÆMIA

Introduction.—The term **Anæmia** has been applied somewhat loosely to denote a variety of conditions, of which the following are the most important :—

1. **Local Anæmia** or **Ischæmia,** *i. e.* where the local blood-supply of an area is diminished, or, it may be, entirely cut off. This condition is described under **Disturbances of the Circulation** (pp. 119 *et seq.*).

2. **Deficiency of the Total Amount of Blood in the Body,** or **Oligæmia.**

3. **Diminution in the Number of Red Blood-Corpuscles,** or **Oligocythæmia Rubra.**

4. **Diminution in the Amount of Hæmoglobin (Achromatosis** or **Hæmoglobanæmia),** either absolutely, or relatively to the number of red cells.

It is to the last three of these, which are morbid conditions of the blood itself, that attention must be given here; and, in any individual case, one or more of these may be present at the same time.

Anæmias have been divided into those the cause of which is known, and which are therefore termed **secondary anæmias;** and those of unknown or obscure origin, which, for lack of more precise knowledge of their causation, are provisionally termed " **primary** " or " **idiopathic.**"

I.—ANÆMIAS SECONDARY TO SOME KNOWN CAUSE

Many possible causes of anæmia might be enumerated, but a description of the following types of **secondary anæmia** will suffice.

Anæmia from Loss of Blood, for example in traumatic hæmorrhage, perforation of a vessel by ulceration (*e. g.* in the wall of a phthisical cavity, or in the base of a gastric or duodenal ulcer, etc.), *post-partum* hæmorrhage, metrorrhagia, hæmaturia, hæmorrhages from mucous membranes, etc.

The results of these conditions, naturally, vary greatly with the amount and frequency of the hæmorrhage.

The immediate danger of a **single large hæmorrhage** is death from lowered blood-pressure. A fatal issue may, perhaps, be averted by making up the bulk of the blood by transfusion, intravenously, or into the tissues, with sterile saline solution. Where this is not done, and when death does not supervene, the lowered pressure within the vascular system induces rapid transudation of the lymph from the tissues into the vessels, and the total **bulk** of the blood may be comparatively rapidly restored if sufficient fluid is available. The blood is at first, therefore, more watery. Later, the bone-marrow and other blood-forming organs take on increased activity in order to replace the lost blood-cells. As has already been mentioned in the section upon blood-formation in the bone-marrow, when such an erythroblastic reaction is brought about, **all** the hæmopoietic activities of the tissue are stimulated, before the marrow steadies down, as it were, to produce the special type of blood-cells required, in this case more particularly the erythrocytes. In this way is explained the occurrence of **post-hæmorrhagic leucocytosis,** as it is called, which is practically a constant phenomenon in such cases, the increase being mainly of the granular leucocytes formed in the marrow, and especially of the neutrophil series. Of these, the polymorphonuclear cells are specially increased, and a varying number of immature cells may also usually be observed.

Even one repetition of a large hæmorrhage may greatly retard an otherwise rapid return to normal, or it may lead to a fatal issue; whilst **repeated small hæmorrhages,** *e. g.* from bleeding piles, menorrhagia, hæmaturia, etc., may produce very severe forms of chronic anæmia indistinguishable from, and perhaps becoming identical with, the so-called pernicious varieties. Albuminuria, over-lactation, chronic suppuration, inanition from starvation, mal-absorption, or other such causes, may, in like manner, lead to serious anæmia.

Secondary anæmias, varying in degree of intensity, may also **follow acute fevers and allied conditions,** especially if these be of prolonged duration, as in the case of typhoid fever. Similarly, anæmia, sometimes very profound, occurs as an **accompaniment** and **consequence of such chronic wasting diseases** or " **cachexias** " as phthisis, syphilis, cancer, malaria (also considered under animal parasites), etc. In several cases recently investigated by Carnegie Dickson, the patients suffered from profound anæmia, diagnosed clinically as pernicious in type, but in which, on *post-mortem* examination, innumerable minute **miliary tubercles** were found throughout the entire bone-marrow. In two of these cases, there was slight old pulmonary tuberculosis, in one case subacute tuberculous peritonitis, and, in another, some old glandular lesions. Carnegie Dickson has also described a somewhat analogous condition of severe anæmia in a case of a young man of twenty-one, from whom a small pyloric carcinoma had previously been removed. No secondary growths were found at

the operation, but, on *post-mortem* examination, the entire bone-marrow was found to be closely studded with innumerable **secondary carcinomatous nodules,** and the intervening marrow-tissue shewed advanced gelatinous degeneration. No secondary growths were discovered in any of the other organs or tissues. **Chronic poisoning** by means of lead, arsenic, mercury, sulphuretted hydrogen, carbon disulphide, T.N.T. (*see* p. 798), and analogous substances, may produce a severe secondary type of anæmia. Anæmias of all grades, up to profound aplastic anæmia, may result from repeated or prolonged exposure of the bone-marrow to the more penetrating varieties of **X-rays.**

Blood-destruction and regeneration has also been extensively studied in **anæmias artificially produced** by the inoculation of animals with phenylhydrazin, saponin, bacterial toxins, tapeworm-extracts, hæmolytic sera, and the like.

Some of the most profound degrees of secondary anæmia known, and frequently simulating pernicious anæmia in type, are those produced by the presence of **certain animal parasites,** especially *Ankylostoma duodenale, Dibothriocephalus latus,* and, in rarer instances, *Trichocephalus trichiuris* and *Oxyuris vermicularis.* The observation that anæmia of this profound nature is not by any means an invariable accompaniment of such infections, and that the symptoms produced by the presence of the three last mentioned of these intestinal parasites are often comparatively slight in degree, has led to the supposition that—for example in cases of *Dibothriocephalus* infection where the resulting anæmia is of a profounder type—it is produced by some **superadded morbid condition of the parasite itself,** whereby certain toxic substances are produced by it within the intestine of its host, from which they are absorbed and thus come to produce their effects. Recovery, in such cases, may occur on expulsion. of the parasite, provided the anæmia has not become too profound.

Some **blood-parasites,** notably those of **malaria,** may also produce serious secondary anæmia, partly from actual using up of the hæmoglobin of the red corpuscles which they infest, and the increased destruction of these cells, and also probably, in part, from the action of certain toxins produced by the parasites.

Methods by which these various causes of Secondary Anæmia may act.—(i) **Diminished Nutrition.**—The digestive and assimilative capacities of the individual may be interfered with, or his food or some of its essential elements may be insufficient to supply material and energy for the hæmopoietic functions of the marrow and other blood-forming tissues. (ii) **Diminished Activity on the Part of the Blood-forming Organs themselves** is an important factor, and may be produced by the action of toxins, poisons such as lead, arsenic, mercury, alcohol, etc., the absence of the stimulus of normal food-products, etc. (iii) Again, **Over-Activity of these Tissues** in one direction, for example in the production of leucocytes of the granular series, as is seen in diseases characterised by leucocytosis, may lead to a corresponding **diminution in**

the output of cells of the red series. Prolonged over-activity, from whatever cause, may also lead to **exhaustion** of the hæmopoietic tissues and consequent failure of their blood-forming powers. (iv) Or again, **diseases such as Syphilis,** which lead to degenerative changes in these organs, may cause a progressive **atrophy** and **failure of their functions.**

(v) **The Increased Destruction of fully-developed Blood-Cells,** in the blood-serum, spleen, liver, bone-marrow, etc., whether brought about by the mechanism of hæmolysis (solution of the red cells), of phagocytosis, or by any other cause, is, of course, an obvious factor in the production of anæmia. Actual loss by hæmorrhage has already been discussed; whilst other causes which may be mentioned are the increased consumption of the albumins of the blood and tissues in fevers and similar conditions: the constant leakage of albumin in albuminuria (in addition to the action of retained toxic substances), etc.

Changes in the Tissues in Secondary Anæmias.—When the anæmia reaches a certain degree of severity, there may occur **multiple hæmorrhages,** varying in size from **petechial** (*e. g.* in the retina or in the subserous or submucous coats in various positions), up to **profuse hæmorrhages,** especially from mucous membranes. The occurrence of **dropsy** is a common phenomenon. In the hæmolytic organs, especially the liver, spleen, and bone-marrow, there may be evidence of the **excessive blood-destruction** in the shape of **pigment,** usually contained within phagocytic cells. This pigment is most commonly in the form of **hæmatoidin;** but iron-containing pigment or **hæmosiderin** may also be present, especially in advanced cases, though not, as a rule, in such quantity as is seen in anæmias of pernicious type.

Blood-changes in Secondary Anæmias.—These naturally vary considerably with the cause, duration, and degree of intensity of the change, and also with the capacity of the hæmopoietic tissues to undergo an erythroblastic reaction. If the loss of blood has been sudden and not repeated, *e. g.* by hæmorrhage, there may be fairly rapid re-formation of blood, especially of its fluid constituents. The **red corpuscles** in secondary anæmias may shew abnormalities in shape (**poikilocytosis**) and size (**anisocytosis**), which, in the less severe types of the disease, may be very slight, or which may be very pronounced when the condition is more intense. In severe cases, **nucleated reds** or **erythroblasts** may appear, owing to the vascular and proliferative changes in the bone-marrow (erythroblastic reaction). In the cases of miliary tuberculosis of the bone-marrow, referred to on p. 614, very large numbers of erythroblasts were present. The nucleated red cells thus occurring in the blood in the severer types of anæmia frequently shew fragmentation of their nuclei, and it is not uncommon to find such cells with nuclei which are somewhat larger and paler, *i. e.* developmentally earlier, than those of the ordinary normoblast; whilst, in certain cases, *e. g.* in *Dibothriocephalus* anæmia, as already mentioned, the changes in the red corpuscles may closely resemble, and be indistinguishable from,

those observed in pernicious anæmia, *i. e.* poikilocytosis, the presence of megaloblasts and megalocytes, etc.

The **leucocytes,** for the reason already mentioned, may be temporarily increased in numbers after hæmorrhage; and, in other instances, leucocytosis, if present, may be due to the disease producing the anæmia. The special types of leucocyte involved will, therefore, in such cases, depend upon the nature of the infective or other cause at work.

The **blood-plates** may be enormously increased, for example they may be found to be three or four times their normal number.

II.--THE SO-CALLED PRIMARY, ESSENTIAL, OR IDIOPATHIC ANÆMIAS [1]

1. CHLOROSIS

Chlorosis is a disease which occurs almost exclusively in young women, especially just after the establishment of the menstrual function, *e. g.* from the age of fourteen to seventeen or later, until that of twenty-four or twenty-five. It is specially characterised by **a relative diminution in the amount of hæmoglobin,** by a moderate diminution in the relative number of red cells per c.mm. (*see* p. 618), and by the presence of some of the other ordinary symptoms of anæmia, *e. g.* dropsy. There is, however, no special tendency to the occurrence of hæmorrhages; and amenorrhœa is usually present.

Ætiology.--Nothing is yet known of the ultimate or essential cause of the condition. Congenital hypoplasia or defective development of the circulatory system and generative organs was thought by Virchow to have some bearing upon it. Others have thought the condition due to diminished capacity for the assimilation of iron. Intestinal auto-intoxication (copræmia) has been considered by some to be the cause, as constipation is a prominent symptom, though whether such constipation is merely a result rather than an ætiological factor is by no means certain. Certain **predisposing factors** in its causation have long been recognised—its occurrence in young women being undoubtedly, in many cases, largely due to the special strain upon the system entailed by the establishment of menstruation; whilst bad food and unhealthy hygienic conditions, and perhaps heredity, are also possible predisposing causes.

The exact nature of the disease is still unknown, but the pathological condition is probably a **functional insufficiency of the bone-marrow**--perhaps in congenitally predisposed subjects, and due to a set of conditions specially found in young women at or just after puberty.

Death in cases of uncomplicated chlorosis is very rare, and, consequently, the lesions in the bone-marrow and other tissues have not been sufficiently investigated. In two fatal cases (one of which died from acute streptococcal septicæmia, and the other from thrombosis of the iliac and renal veins), which one of the authors has had the opportunity of examining, there was wide-spread gelatinous degeneration of the marrow, with diminution in the amount of

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[1] As previously indicated, these are merely provisional terms indicating that the causes are as yet unknown (*see* p. 613).

hæmopoietic tissue, though whether these changes are present in uncompli-
cated cases we have not sufficient grounds for stating.

The skin shews a greenish-yellow tinge; and there is sometimes slight
increase of pigment in parts. The subcutaneous fat may be normal in
amount or even present in excess.

In the majority of anæmias, the **total mass** of the blood is usually
diminished, but in chlorosis the fact has been established, by the method
of Haldane and Lorrain Smith, that the **total mass is usually, and often
remarkably, increased**—a fact which must be borne in mind in interpreting
the blood-count and estimation of hæmoglobin in this disease (*see* p. 617).
It is said that the **plasma** may even be doubled in total bulk (Haldane),
and yet its specific gravity is usually not only not diminished, but is
normal or even slightly increased—though the specific gravity of the blood
as a whole is reduced, owing to the deficiency of red corpuscles.[1] This
increase in the amount of plasma has been regarded by some as the
essential factor in the production of chlorosis, but the disease is not
cured by its reduction unless, at the same time, iron is administered.

The blood is distinctly pale in colour, and the most important patho-
logical change in it is the marked **diminution in the amount of hæmo-
globin present,** *e.g.* forty per cent., thirty per cent., or even twenty per cent.;
whilst the **number of red cells** may not be very much below normal, *e.g.* **four,**
or in severe cases **three-and-a-half** or **three millions** or less per c.mm.

The **erythrocytes** may shew some, and, in severe cases, considerable,
poikilocytosis and **irregularity in size,** usually in the direction of diminu-
tion rather than of increase; but their most characteristic feature is the
pallor of their centres, from deficiency of hæmoglobin, as may be well
seen in Plate XVI, fig. 2.

Occasional **nucleated red cells** may be found, their number varying
considerably from time to time even in the same case. They are usually
found in the severer cases.

The **leucocytes** do not exhibit any characteristic changes. They may
be diminished, but are more usually normal or slightly increased in
numbers; and, in a series of cases examined by one of the authors, this
increase was distinct.

The **platelets** are usually somewhat increased. The **specific gravity**
of the blood (which, in the healthy adolescent female, may be normally
somewhat under 1·055) may fall to 1·035 or even 1·030. The **alkalinity**
appears not to be particularly altered, but the **coagulability** is distinctly
greater than in other anæmias of equal degree—an important point in
connection with the occurrence of **thrombosis** which has frequently been
described in chlorosis, *e. g.* in the femoral or other veins, cerebral venous
sinuses, and even, though rarely, in arteries.

The condition rapidly improves on giving iron, and is practically
never fatal, unless from the occurrence of venous thrombosis, or some
intercurrent malady.

[1] See note, p. 569.

2. PERNICIOUS ANÆMIA

This important disease, or rather group of diseases, as it should probably be regarded, is also, from the fact that we are still ignorant of its ultimate cause, sometimes known as " **Essential** " or " **Idiopathic** " or " **Primary Pernicious** " **Anæmia.** The term " **Progressive Pernicious Anæmia** " is also frequently employed to denote the progressive and almost uniformly fatal character of the disease. It is usually insidious in its onset, and is characterised by typical changes in the blood, in the bone-marrow, and in some of the other organs : and by certain clinical symptoms, such as the lemon-yellow colour of the skin, a varying degree of breathlessness, vomiting, and other digestive disturbances, irregularities in temperature, and—when the anæmia reaches a certain stage—by hæmorrhages, e. g. into the retina, serous membranes, etc., or from mucous surfaces.

Ætiology.—The disease is specially one of adult life, and the sexes are practically equally liable. As already stated, the ultimate cause of the disease is still entirely unknown ; but, in recent years, the causes of certain types of anæmia closely resembling, and clinically indistinguishable from, it, have been definitely established. Reference has already been made to several of these **secondary anæmias of pernicious type,** particularly those produced, under certain conditions, by some intestinal parasites, e. g. *Dibothriocephalus latus, Ankylostoma duodenale,* and, in rare instances, *Trichocephalus trichuris* and *Oxyuris vermicularis.*

Other forms of secondary anæmia, very closely **resembling** the " true " progressive or primary pernicious form, are sometimes found in cases of gastric cancer, syphilis, and malaria, in wide-spread secondary malignant involvement, and in miliary tuberculosis, of the bone-marrow (*see* pp. 614 and 616), and also following the administration of certain poisonous drugs ; but it is usually, though not always, possible to differentiate these by a careful examination of the blood.

Certain phenomena characteristic of the disease have from time to time been put forward as **causal,** but are rather to be regarded as **consequences** of some as yet unknown cause, probably toxic in its nature. In this category may be placed **excessive hæmolysis,** characterised by active **phagocytosis of red corpuscles** in the bone-marrow, spleen, and other hæmolytic organs, and by the **deposit of pigment** (mostly in the form of hæmosiderin) in the liver, kidneys, bone-marrow, spleen, etc. Similarly, the **defective**—or rather **active but aberrant—hæmatogenesis** is a result of the action of some toxic or other agency, rather than itself a cause of disease; and the erythroblastic, and more especially the megaloblastic, type of transformation of the bone-marrow, so characteristic of pernicious anæmia, is a **reaction** of the tissue produced by some unknown cause. Such cause has been sought for in various directions, and many authorities consider that pernicious anæmia is probably brought about by some

toxin produced in, and absorbed from, the alimentary canal. Hunter [1] is of opinion that "Pernicious anæmia is a chronic infective disease localised in the alimentary tract; caused by a definite infection of the alimentary tract, chiefly of the stomach, occasionally also of the mouth, and of the intestine." He supposes that "the chief source of the infection is oral sepsis arising in connection with long-continued and neglected cario-necrotic conditions of teeth; sometimes, possibly, arising from other causes." Long-continued pyorrhœa or suppuration of the gums and teeth-sockets is a not unlikely cause in some cases. Other writers hold the view that the disease arises from various lesions, functional disturbances, or specific infections of the gastro-intestinal tract. It has also been said that repeated hæmorrhages, e. g. from piles, abnormalities of pregnancy and parturition, and long-standing secondary anæmias may sometimes precede its appearance.

Changes in the Blood.—The blood may be pale and watery; its **specific gravity** is lowered, and may fall even below 1·030; its **total bulk** is lessened; and its **coagulability** is much diminished.

The **red corpuscles** shew a great and progressive **diminution in numbers,** for example to about 1,000,000; and, in many advanced cases, the count may lie between 600,000 and 300,000 per c.mm., and even lower counts are occasionally obtained. The corpuscles do not tend to form rouleaux. **Poikilocytosis** (Plate XVI, fig. 1) is a marked and constant feature, as are also great alterations in the **size** of the corpuscles. Unusually small forms or **microcytes** are often present, but the abnormal cells most characteristic of the condition are **megalocytes** and **megaloblasts,** especially the latter, which, after early infancy, are found in any appreciable numbers in the blood only in this condition and in a few secondary anæmias of pernicious type, such as the *Dibothriocephalus* anæmia above referred to. Certain of these non-nucleated and nucleated red cells are of such large size—e. g. exceeding even 20 μ in diameter—that the terms **gigantocyte** and **giganto-blast** have been applied to them. Normoblasts may also be found, but are seldom very numerous except in advanced stages of the disease. The number of nucleated red cells in the blood may, in some cases, increase remarkably after transfusion. Both megaloblasts and normoblasts may exhibit **karyorrhexis** or **nuclear fragmentation,** and, very occasionally, true mitosis may be observed in them. The various forms of red cell frequently shew other **degenerative changes,** *e. g.* **polychromatophilïa, punctate basophilia** or **granular degeneration,** as well as the poikilocytosis already mentioned (*see* Plate XVI, fig. 1).

Although the total amount of **hæmoglobin** present in the blood may fall to thirty per cent. of the normal or less, yet, in relative proportion to the number of red cells present, it may not only not be diminished, but the **amount per corpuscle** may even be increased, and the **colour-** or **hæmoglobin-index** is frequently above unity and may reach 1·5, or even 1·8,

[1] Hunter, *Pernicious Anæmia : Its Pathology, Septic Origin, Symptoms, Diagnosis, and Treatment,* London, 1901, Griffin & Co., p. 245. Also numerous papers in *Lancet* and *British Medical Journal.*

a phenomenon due in part to the larger size of many of the red corpuscles, as well as to an actual condensation of their contained hæmoglobin.

The **leucocytes** are, as a rule, distinctly, and sometimes markedly, diminished in numbers, especially the **polymorphs,** owing to the energies of the marrow being directed towards the production of cells of the erythroblastic series. Leucocytosis may, however, occur from the presence of intercurrent or terminal infections and complications such as pneumonia, **Eosinophil cells,** although often present in considerable numbers in the marrow, are not, as a rule, specially increased in the circulating blood. If present in the latter in abnormally large numbers, the possibility of the case being **parasitic** should be borne in mind. The **lymphocytes** may be relatively less diminished in number than the polymorphs.

The number of the **blood-platelets** is usually much decreased.

The condition is, therefore, a **megaloblastic anæmia** characterised by marked diminution in the numbers of **all** the formed elements of the blood.

Changes in Other Organs and Tissues :—

Bone-Marrow.—The changes which occur in this tissue are extremely characteristic. They are chiefly of the nature of a marked **erythroblastic reaction,** usually pronouncedly **megaloblastic** in type (see Plate XVI, fig. 4). In advanced cases, megaloblasts may form the majority of the total cells present, and are usually far in excess of what might be expected from the examination of the blood. This megaloblastic condition of the marrow may, indeed, in some cases be present, where very few cells of this type had been observed in the circulating blood before death.

Myelocytes and other cells of the leucocyte-forming series are usually much diminished in numbers, although the capacity for leucoblastic transformation is generally retained, and may shew itself in cases where pneumonia or some such leucocytosis-producing complication supervenes. As already mentioned, eosinophil myelocytes are often numerous in the marrow in pernicious anæmia.

Another phenomenon, of constant occurrence in the marrow in this disease, is the presence of large numbers of **actively phagocytic cells** engaged in the process of blood-destruction or hæmolysis (see Plate XIV, fig. 4). These cells may contain enormous numbers of red corpuscles, both nucleated and non-nucleated ; or, in other instances, they may be filled with blood-pigment derived from these. The red cells are not only hastily and imperfectly formed in excess, but are also destroyed in excess. These hæmolytic processes in the marrow, if the amount of this tissue throughout the body be taken into account, form an extremely important aspect of the disease not yet sufficiently recognised.[1]

[1] See Carnegie Dickson, The Bone-Marrow: A Cytological Study forming an Introduction to the Normal and Pathological Histology o, the Tissue, more especially with regard to Blood-Formation, Blood-Destruction, etc. Longmans, Green & Co., 1908.

The fatty tissue of the marrow disappears, and the medullary cavities of the bones become enlarged by the absorption of the spongy, and even of much of the compact, bone. The marrow is much redder in colour, and its appearance has suggested the comparison to red-currant jelly or raspberry jam. Where much blood-pigment is present, it may be brick-red in colour; or, where leucocytosis is superadded from the presence of some complication such as pneumonia, it may be of a pinkish or pale-red tint.

Liver.—The organ may be normal in size or slightly enlarged, the individual lobules being often increased in dimensions, and exhibiting distinct outlines. It has a characteristic **brownish-yellow** or *café-au-lait* tint, due to the combined presence of **pigmentation** and **fatty degeneration.** The **Prussian-blue reaction** with hydrochloric acid and potassium ferrocyanide is used to demonstrate the presence of the **hæmosiderin,** an iron-containing pigment derived from the hæmoglobin of the destroyed blood-corpuscles. This is present in the form of small granules in, and to a less extent between, the liver-cells, especially at the peripheral parts of the lobules next the portal tracts, where it forms a darker zone which maps out the lobules distinctly. The quantity of iron contained in such a liver may, it is said, be as much as nine or ten times the normal amount.

Spleen.—This organ may be slightly enlarged in some cases. It has, usually, a somewhat dark brownish-red colour, and may not give the typical Prussian-blue reaction, the reagents often producing a variable greenish- or bluish-black discoloration. **On microscopical examination,** marked increase of hæmolytic activity is demonstrated by the presence of **active phagocytosis,** especially on the part of the endothelial cells of the pulp, these cells often attaining a large size and containing numbers of ingested red corpuscles and pigment-granules.

Kidney.—The kidneys are usually of a pale brownish-yellow tint, from the presence of **hæmosiderin**-pigment, combined with intense **fatty degeneration** in the cells of the convoluted tubules and ascending or secreting parts of Henle's loops.

Heart.—This generaliy shews very profound **fatty degeneration.** The condition is usually most advanced in the inner part of the muscle of the left ventricle. It is often distinctly patchy in its distribution, and may shew through the endocardium as irregular yellowish-white spots or patches, usually best seen on the papillary muscles and inter-ventricular septum—the so-called " thrush-breast " or " tabby-cat " appearance.

The **lungs** commonly shew a condition of **atrophous emphysema.** The **endothelium of the smaller vessels and capillaries,** e. g. in the pia, omentum, etc., may shew wide-spread **fatty degeneration;** and **hæmorrhages** may be found, e. g. in the retina, subcutaneous tissues, serous and mucous membranes, central nervous system, etc.

In the **central nervous system,** especially in the cord, various degenerative lesions have been described, for example, sclerotic changes, especially

in the posterior columns (see under **Subacute Combined Sclerosis,** p. 1006). These may be associated with the occurrence of hæmorrhages, and are probably due to the action of some toxic substance circulating in the blood.

The **gastric** and **intestinal mucous membranes** frequently shew a condition of advanced atrophy.

The **fat of the body** is usually of a bright yellow tint.

THE BLOOD IN GENERAL DISEASES

The condition of the blood in the **Acute Infective Fevers,** and in **Septicæmias** and similar conditions, has already been sufficiently dealt with under **Leucocytosis and the Reactions of the Hæmopoietic Tissues,** especially the **Bone-Marrow.** For a fuller account of such changes, and the alterations found in the blood in general diseases such as **Myxœdema, Exophthalmic Goître, Tuberculosis,** etc., special works on Hæmatology should be consulted.[1]

BLOOD-CHANGES IN MALIGNANT DISEASE

One of the most important points to be noted in the study of the blood in malignant disease is the great **variability** of the findings, not only between those in different varieties of tumours, but also according to the site, size, and rapidity of their growth, the occurrence of metastases, the position of these in the body, and the supervention of inflammatory changes, necrosis, hæmorrhage, etc. The age and previous health of the patient are also important factors, and great individual variations occur where the characters of the disease are apparently more or less similar. It is, therefore, impossible as yet to lay down definite rules with regard to the blood-changes in any given case or set of cases, but the following generalisations may be useful.

Simple tumours, unless the seat of inflammatory processes such as ulceration, or unless they interfere with nutrition (*e. g.* by obstruction of the œsophagus by pressure), usually produce little or no appreciable alteration in the blood. The same is generally true of **small, slow-growing malignant tumours.** With **large, rapidly-growing tumours,** however, it is otherwise, especially if metastasis occurs.

In Cancers of this description, a **secondary anæmia,** varying in severity from a mild to a very severe type, may be present. A common degree of such anæmia is where the red corpuscles number about four to three-and-a-half millions, but, in severe cases, they may fall to a much lower figure, and

[1] Ewing, *Clinical Pathology of the Blood,* Kimpton, London, 2nd edition, 1904.

Cabot, *Clinical Examination of the Blood,* Longmans, Green & Co., London, 5th edition, 1904.

Carnegie Dickson, *The Bone-Marrow,* Longmans, Green & Co., London, 1908.

Gulland and Goodall, *The Blood : A Guide to its Examination and to the Diagnosis and Treatment of its Diseases.* W. Green & Son, Ltd., Edinburgh. Second Edition, 1914.

come to simulate the condition in pernicious anæmia. The red córpuscles appear to be more delicate and more easily destroyed than usual. **Poikilocytosis** frequently occurs, and, in some cases, may be very extreme. **Nucleated reds** are common, and are usually normoblastic in type, though megaloblasts are occasionally found in severe and advanced cases. The **colour-index** is usually low in proportion to the number of red cells, *i. e.* they are pale and poor in blood-pigment, even when a comparatively high count is found. The **specific gravity** of the blood is lowered, being usually roughly parallel with the amount of hæmoglobin present. **Coagulability** is generally little altered or, perhaps, slightly decreased. Where the bone-marrow itself is the seat of wide-spread secondary growths, a progressive anæmia, aplastic in type, may be found, which, in some cases, may come to simulate pernicious anæmia.

Considerable attention has been given to the question of the **presence or absence of leucocytosis** in cases of cancer; and here, again, the results of investigation shew wide divergence in different cases, according to the nature and site of the tumour and the occurrence of secondary changes in it, and the other variable factors already mentioned. Leucocytosis may be absent or slight where the tumour is small and slow-growing; but, where growth is rapid, and especially if wide-spread metastasis occurs, marked increase of white cells, particularly polymorphs, may be found. In microscopical sections of such tumours, at the spreading margins, and in areas shewing necrotic softening, there is, not infrequently, a certain, and, in some cases, a considerable, degree of polymorphonuclear infiltration. Similarly, where ulceration or other inflammatory processes supervene, leucocytosis resembling that due to ordinary inflammation, with regard both to the number and character of the white cells, is produced.

In some instances, however, notably in cancer of the œsophagus, unless inflammation or secondary spread occurs, the number of the leucocytes may not only not be increased, but may be actually diminished, probably from interference with nutrition.

Leucocytosis tends to occur in cases where there is **hæmorrhage,** *e. g.* in gastric and uterine cancers. It is also said to be specially pronounced in **cancer of the kidney** (Cabot), **pancreas,** or **thyroid.**

In **cancer of the stomach,** *without* hæmorrhage, ulceration, or metastasis, leucocytosis is relatively infrequent, and the normal digestion-leucocytosis, occurring after a meal, is usually absent—a phenomenon which, however, is of only relative importance, as a similar absence of digestion-leucocytosis has been observed in catarrhal conditions of the stomach, and in cases of debility from other causes.

In **cancer of the liver,** distinct leucocytosis is present in rather more than half the cases, especially in their later stages; and, in these cases, there is usually also marked anæmia, with diminution in the amount of hæmoglobin.

In **intestinal carcinoma,** the records are extremely variable, though

an increase of white cells is usually to be observed in most cases of cancer of the abdominal organs, probably from the ready occurrence of hæmorrhage and secondary inflammatory changes.

In the case of mammary cancers, moderate leucocytosis is frequently present, but its presence and degree are extremely variable.

On comparing the blood-changes above detailed for cancer with those found in sarcoma, it may be said that, on the whole, they are somewhat similar, but usually rather more constant and more pronounced in the latter class of malignant tumours. The red corpuscles are, as a rule, diminished, e. g. to four or three millions or less, the hæmoglobin-percentage, averaging about fifty per cent., though it may fall much lower. The white cells, though in a few cases they may remain practically unaltered, more commonly exhibit a rise to fourteen or fifteen up to forty or fifty thousand, or even more. This increase, though usually mostly of the polymorphonuclear cells, may occasionally be largely a lymphocytosis, especially in certain sarcomatous affections of lymphatic glands (see p. 611). The occurrence of a few myelocytes in the count is comparatively common. As in the case of cancer, there may be little alteration in the blood where the sarcomatous growth is small, slow-growing, and without metastasis.

After the operative removal of a malignant tumour, the leucocytosis, if present, usually gradually disappears; and its return may herald the regrowth or recurrence of the disease.

HÆMORRHAGIC DISEASES

HÆMORRHAGES, in and from serous and mucous membranes, in the skin, etc., varying in size from those of petechial dimensions up to large effusions, may occur in various diseases. These may be " symptomatic " or secondary to some known or unknown cause : for example, the so-called " symptomatic purpura " seen in many infective diseases such as pneumonia, cerebro-spinal fever (for this reason often called " spotted " fever), pyæmia, acute liver-atrophy, the septicæmias, smallpox, etc. Hæmorrhage into the medulla of the suprarenals is frequently seen in cases of diphtheria, cerebro-spinal fever, typhus and certain other acute diseases. Such hæmorrhages are probably due to the deleterious action upon the blood-vessels of the toxins of these diseases (cytotoxins, endotheliolysins, etc.—see Immunity, pp. 468–9; and also cf. p. 284). Similarly, hæmorrhages may be due to the action of poisonous drugs (e. g. iodides), snake-venom, and certain other animal and vegetable poisons; and they may occur in the auto-intoxication of jaundice—probably from the action of the bile-acids—and in any severe grade of anæmia, and in some cachexias. They are also described as occurring in certain nervous diseases. Mechanical causes which bring about great venous engorgement may produce them, e. g. strangulation, drowning, etc.

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There remain certain cases in which all these recognisable causes can be eliminated, and in which hæmorrhages occur from ætiological factors which have not yet been ascertained. Such cases, according to their outstanding features, have been grouped under certain names, the most important of which are **Purpura Hæmorrhagica, Hæmophilia,** and **Scurvy.**

PURPURA HÆMORRHAGICA (Werlhoff)

This is a disease, varying in severity, and occasionally very rapid and fatal in its course, in which numerous smaller or larger hæmorrhages occur. These may take place into, or from, practically any of the tissues or organs of the body, but are specially liable to occur in the **skin** and from **mucous membranes.** In many of the reported cases, various **bacteria** such as *Strepto-* and *Staphylo-cocci, Pneumococci,* anthrax-like bacilli, and other organisms, have been isolated; but, in other cases, the bacteriological examinations have been negative. Ewing suggests that these latter cases are probably acute manifestations of **Hæmophilia.** Other writers describe lesions in the suprarenals, especially hæmorrhages, and are inclined to regard them as causing the hæmorrhages elsewhere. These may, however, merely be themselves symptomatic.

In all cases of purpura, there is **anæmia,** which may become very profound, and which is accompanied by great **diminution of hæmoglobin. Polymorphonuclear leucocytosis** is found in the infective cases, but is generally absent in the hæmophilic type. **Affections of the joints** are common, a fact which has led to some cases being termed **Rheumatic Purpura.**

Various hæmorrhagic conditions may occur in **infancy and early childhood,** some of them resembling **purpura hæmorrhagica.** In certain of these, **syphilis** appears to play an important part, whilst others, *e. g.* **epidemic hæmoglobinuria** and **melæna neonatorum,** are probably due to, as yet unknown, infective agents. In **congenital obliteration of the bile-ducts,** hæmorrhages are of frequent occurrence, as in other diseases accompanied by jaundice.

The **coagulability** of the blood does not appear to be specially altered, but **retraction of the clot** is said to be deficient (Hayem).

Henoch's Purpura, a condition which may occur at any age, but which is relatively more frequent in children, is characterised by more or less acute abdominal symptoms, such as colic, vomiting, and hæmorrhages into the walls and lumen of the stomach and intestines, together with pain and swelling in the joints, and a purpuric skin-eruption. The attacks may be recurrent, and the patient may die from peritonitis or other complications.

HÆMOPHILIA, OR " HÆMORRHAGIC DIATHESIS "

Persons who suffer from this disease—usually young males—appear to be hereditarily predisposed to the occurrence of hæmorrhages, which

may be extremely severe, and even fatal, and may arise from the most trifling injury, such as a blow, a scratch or small cut, or the extraction of a tooth, or even without any evident exciting cause. The work of Wright and others has shewn that the **coagulation-time** of hæmophilic blood is **increased**—sometimes greatly so. Many hypotheses as to the reason for this delay have been advanced, such as diminution in the calcium-content of the blood, etc. Addis,[1] in his work on hæmophilia, however, states that the calcium-content is *not* diminished. He considers that : " the proximate cause of the delay in coagulation is the **slowness of the formation of hæmophilic thrombin,**" owing to a **qualitative** (but not quantitative) **alteration in the prothrombin,** which reveals itself in the longer time required for the change into thrombin (*see* p. 570). He discovered no appreciable abnormality in the other factors, viz. the amount and coagulability of the **fibrinogen,** and in the amount and activity of the **thrombokinase** and **calcium;** and he found no substance in hæmophilic blood, not present in normal blood, which hinders the formation of thrombin. The disease, as stated above, specially affects males, and appears to be transmitted by the mother. Beyond a slight diminution in the number of the leucocytes, especially the polymorphonuclears, described by Wright, no characteristic histological changes in the blood or organs have yet been demonstrated.

SCURVY, OR SCORBUTUS

This disease consists of a severe **anæmia,** unaccompanied by leucocytosis, unless from the presence of some inflammatory or other complication. It is characterised by great **debility, spongy swelling of the gums, pyorrhœa, loosening and falling-out of the teeth,** and **bleeding** from the swollen gums and elsewhere. **Subperiosteal** and **intramuscular hæmorrhages** are frequently found, especially in the lower limbs. Scurvy arises as a result of unsuitable food and unhealthy hygienic conditions of life, and specially attacks badly-fed soldiers or sailors who are exposed to hardships under unfavourable conditions with regard to light and air, and who are deprived of fresh vegetables in their diet. It is doubtful whether these conditions alone are capable of producing the disease, or whether there is also an infective agent at work; but, unless the cases have already progressed too far, recovery is usually rapid when fresh vegetables, lemon-juice, and fresh, in place of tinned or salted, meat —*i. e.* substances containing the necessary vitamines—are added to the patient's dietary, and he is placed in healthy surroundings.

An **Infantile form of Scurvy** (Barlow's disease) occurs, most commonly in weakly, hand-fed infants, especially if also in bad sanitary surroundings. In these, the disease closely resembles the condition found in the adult;

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[1] Addis, "The Pathogenesis of Hereditary Hæmophilia," *Jour. Path. and Bact.,* vol. xv., No. 4, p. 427.

and hæmorrhages, especially under the periosteum and into the soft tissues of the orbits and eyelids (producing proptosis, " black-eye," etc.), are common. Rarefaction of the bones, often leading to fracture, is usually present, and the condition is frequently associated with the occurrence of rickets.

[NOTE.— *Certain diseases of the blood, characterised especially by changes in the* **Spleen,** *will be found described in the next chapter.* **Agglutination** (p. 472), **Hæmolysis** (p. 468), etc., of red blood-corpuscles, and analogous phenomena, are dealt with in the Chapter on **Immunity.** The problems connected with **Thrombosis** are also considered under **Thrombosis,** pp. 137 *et seq.*]

DISEASES OF THE LYMPHATIC SYSTEM

SEROUS MEMBRANES

DISEASES of these structures are described under their respective systems (*see · under* **Pericardium, Pleura, Peritoneum,** etc.).

LYMPHATIC VESSELS

LYMPHANGITIS, or inflammation of lymphatic vessels, may be **acute** or **chronic.** The acute condition is the result usually of **septic infection,** *e. g.* in dissection or *post-mortem* wounds and similar conditions. The inflamed lymphatics are seen upon the surface, *e. g.* of the arm—in a case of poisoned wound, say, of the finger—as narrow, bright red, more or less straight lines, running from the focus of infection towards the nearest groups of lymphatic glands—in this instance the epitrochlear and axillary. The changes in and around these vessels are very similar to the phenomena seen in inflammation of veins, viz. inflammatory swelling of the intimal endothelium and the other coats of the vessels, leucocyte-infiltration and œdema of the surrounding tissues (perilymphangitis), and, perhaps, thrombosis of the lymph in the lumen of the vessel. The proliferating cells of the endo- and peri-thelial coats of lymphatics are an important source of the large mononuclear cells of exudates in many inflammatory conditions. Long continued or repeated attacks may lead to **chronic lymphangitis,** a condition which is seen in an exaggerated form in **elephantiasis** (*see* p. 435).

Chronic lymphangitis is often due to some **specific infective agent,** especially the organisms of tuberculosis, syphilis, glanders, and allied diseases. **Tuberculous lymphangitis** is well seen in the subperitoneal lymphatics and lacteals which become infected from a tuberculous ulcer of the intestine, where they may be observed as whitish lines dotted with small tuberculous granulations. In **glanders,** the lymphatic trunks are specially affected, and shew as thickened cord-like masses—the so-called **farcy-pipes** seen in the horse.

LYMPHANGIECTASIS.—Congenital lymphangiectasis may occur in various forms, *e. g.* in a more or less circumscribed form in **lymphangiomas** (*see* p. 321), or in a more or less diffuse variety affecting the tongue (**macroglossia**), lip (**macrocheilia**), or vulva.

In its acquired form, the condition seldom arises from obstruction of

the flow in the lymphatic channels. In cases of **filarial infection,** however, the presence of the adult worm, *Filaria bancrofti,* may produce an irregular varicose condition of the lymphatics of the groin, pelvis, and abdomen; or the impaction of the prematurely discharged ova or coiled-up larvæ of the parasite may lead to wide-spread obstruction of the smaller lymph-channels, this—along with recurring inflammatory attacks—producing the condition of **elephantiasis.** The lymphatics may rupture and lead to the escape of chyle, *e. g.* in filarial infection, giving rise to **chylous ascites, chyluria, chylocele,** etc., according to the site of rupture (*see* p. 435). Chylous ascites may also occasionally arise from the pressure of tuberculous glands, etc., upon the receptaculum chyli.

Dilatation-cysts, usually minute in size, are very common upon the lacteals in the intestinal wall or mesentery, and may be recognised by their milky, fluid contents.

NEW GROWTHS.—Primary tumours of lymphatic vessels are some-what rare. They are usually congenital, and may occur as **plexiform,** or, more commonly, as **cavernous, lymphangiomata,** *e. g.* in the skin and subcutaneous tissue, or, very rarely, in the ovary, hilus of the kidney, and elsewhere. Occasionally, they may be combined with adenomatous tumours, *e. g.* in connection with the parotid, pituitary, and other glands. **Cystic tumours** of lymphatics or **hygromas** may be found about the neck, face, and elsewhere. Cystic formations may also occur in connection with serous membranes, usually as diverticula which may become shut off from the main sac, *e. g.* **ganglia** in the case of synovial membranes.

Secondary infiltration along lymphatics is very common in the case of malignant tumours, especially cancers and melanotic sarcomas.

LYMPHATIC GLANDS

The lymphadenoid tissue of the body is not found, only in the form of **lymphatic glands,** but also in the **Peyer's patches** and **solitary follicles of the intestine, lymphoid tissue of the tonsils** and **pharynx,** the **bronchial lymphoid sheaths, periarterial lymphoid tissue of the spleen** (Malpighian bodies), **mesentery,** and elsewhere, and in the **thymus gland** before it atrophies. In all of these, the lymphadenoid tissue may be affected and react in very much the same way in various pathological conditions, the differences depending mainly upon the anatomical distribution of the tissue.

Practically all the lymphatic trunks draining the tissues of the body pour their contents into the lymphatic glands, which are arranged usually in groups. These act as filters for the lymph as it passes through them into the efferent vessels, and they are therefore specially liable to infection by bacteria or other infective organisms carried in the lymph, as well as to the deposit in them of tumour-cells, and of pigment or other particulate substances brought to them in the same way.

. The **afferent lymphatics,** before entering the substance of the gland, break up into a fine network upon its surface. From this, the lymph is carried by fine channels into the **lacunar system of lymph-sinuses in the cortex,** and then through a similar network in the medulla, from which it is collected by several channels which unite in the hilus of the gland to form the **efferent lymphatic**

vessel. Organisms, tumour-cells, and particulate substances brought by the **lymph-stream** are thus specially liable to be caught in the surface plexus, in the sinuses of the cortex and medulla, or in some other part of the filtering system alluded to; whilst similar substances brought by the **blood-stream** are more likely to affect the lymph-follicular system of the gland, on account of the fact that the arteries, after entering the gland and running in the trabeculæ, are distributed mainly to this element of the glandular structure. For this reason, the lymph-follicular tissue is also very readily affected by anything causing hyperæmia of the glands, and by inflammatory, septic and toxic conditions acting through the blood-stream. The **reticulum** of both the lymphadenoid and the sinus systems is composed of fine cells with branching and anastomosing processes and fibres, around which are wrapped flattened endothelial cells which readily react in certain pathological conditions. In the **lymphadenoid areas** (lymph-follicles or cords), the meshes of this reticulum are occupied by the closely packed **lymphoid cells** or **lymphocytes.**

Fig. 283.—Section of Normal Lymphatic Gland. In the capsule are seen sections of the plexus formed by the afferent lymphatics. The darker areas are the lymph-follicular cords, to which a small artery is seen passing (in centre of section). The paler areas are the lymph-sinuses. × 50.

The classification of diseases characterised by enlargement of the **lymphatic glands,** or of the **spleen,** or of these structures together, is a problem of great difficulty; and, frequently, it is only by examination of the blood that such cases can be differentiated from one another. Thus, in their clinical history and naked-eye morbid anatomy, some cases of **lymphadenoma** or **Hodgkin's disease** closely simulate **leucocythæmia,** whilst, in other respects, they closely resemble **chronic infective glandular overgrowths** such as may occur in **tuberculosis, syphilis,** and similar conditions. In other instances, it is difficult to differentiate cases of

lymphadenoma from true **tumour-formations** *such as* **lymphomas** and **lymphosarcomas ;** *whilst cases of* **splenic anæmia** *form another group* which must be differentiated from them.

Whether these diseases should be classified as morbid conditions of the blood, or as diseases of the lymphatic glands and spleen, is a much debated point, but, as has already been indicated when discussing pernicious anæmia and the leukæmias, many conditions formerly described and classified as " primary blood-diseases " must now be regarded as manifestations of certain **reactions in the blood-forming tissues, produced by infective or other causes** of known or unknown nature. Much of what has already been said with regard to the rôle played by the bone-marrow in such conditions may, therefore, also be applied to the hæmopoietic tissues concerned with the production of the lymphocytes, viz. the lymphatic glands, spleen, and lymphoid tissues generally; but it must be borne in mind that these tissues, just as in the case of the marrow, also possess important **phagocytic, cytolytic, and other functions,** which may become exaggerated or perverted under pathological conditions.

ATROPHY of lymphatic glands, and of lymphoid tissue generally, is found as a **senile** condition. It is accompanied by fibrosis of the gland-tissue, with diminution in the number of lymphocytes—of which there is less active proliferation—associated with the diminished metabolism of old age. Similar senile atrophic changes are found in the Malphigian bodies of the spleen, in the Peyer's patches and solitary lymphoid follicles of the intestine, and in lymphoid tissue elsewhere. The lymphatic glands become smaller and firmer, though their bulk may be partly maintained by the infiltration of certain areas with fat —a phenomenon also observed not infrequently in, say, the axillary and other glands in the neighbourhood of scirrhus cancer of the breast, quite apart from, as well as in association with, any phenomena due to secondary infiltration of the glands with tumour-tells. Atrophy of the lymphadenoid tissues, in association with atrophy of other tissues, is also seen in many **wasting conditions,** and is often very marked in **marasmic** infants and children.

WAXY or AMYLOID DEGENERATION.—The lymphatic glands are a not infrequent seat of this change. The glands may be enlarged and indurated. **On section,** they may shew little apparent alteration to the naked eye, and require microscopical examination with special staining reagents; or they may present a pale, whitish, shining appearance, with small translucent points which stain dark brown with iodine. The change is usually most marked in the connective tissue around and in the walls of the arterioles and the capillaries arising from them. It is best seen, therefore, at the centres of the lymph-follicles, where these vessels are situated. The degeneration affects also the fibres of the adenoid reticulum. The affected structures shew the usual homogeneous swelling, and the characteristic staining reactions with methyl violet,

etc. The intervening cellular elements, especially the lymphocytes, *become correspondingly compressed and atrophied.*

PIGMENTATION.—Foreign particles may be carried to; and deposited in, lymphatic glands, which, as already explained, act as filters for the lymph-stream. Such particles are usually contained within phagocytic cells—polymorphonuclear or mononuclear, as the case may be. These cells, which have taken up such pigment from the area drained by the lymphatics passing to some gland or group of glands, carry the particles to these glands, and may either deposit their contained particles in them, or may themselves, along with their contents, be englobed by the **actively phagocytic endothelial cells** lining the lymph-sinuses, etc. Such particles are deposited, first in the peripheral network on the surface of the gland, then in the lymph-sinuses of the cortex and of the medulla. They may also be found later in the lymphoid follicular tissue of the cortex; and, lastly, the whole glandular structure may be crowded with pigment. The commonest variety of such glandular pigmentation is to be seen in the **bronchial glands,** to which particles of **carbon** inhaled into the lung are carried. A considerable degree of such pigmentation is present in practically all town dwellers, but it occurs in its most exaggerated form in **anthracosis** or coal-miners' disease, in cases of which the pigment is not only carried from the lung to the bronchial glands, but it may be found in the mediastinal and abdominal glands, and, in extreme cases, in practically all the lymphatic glands of the body.

Particles of **stone** and other pigments may be found under similar circumstances. In **tattooing,** a large part of the pigment introduced under the skin is carried by phagocytic cells to the neighbouring lymphatic glands. In the same way, large quantities of **blood-pigment** may be found in glands near hæmorrhages or wounds.

Such pigment, of whatever nature, is usually contained **within cells—** first in the phagocytic wandering cells which bring it to the gland, and then in the endothelial cells lining the lymph-sinuses. When pigmentation of the follicular tissue occurs, the particles are often deposited and found free.

The presence of pigment leads to **proliferation of the endothelial cells** of the sinuses, and to progressive **thickening of the reticulum,** apparently from defective nutrition from interference with the functions of the investing cells which govern the nutrition of the fibres. These changes lead to **compression-atrophy of the lymphoid cells,** and may end in complete **fibrosis** of the whole gland-structure.

LYMPHADENITIS.—Acute inflammatory changes are very common in lymphatic glands, as these structures are, from their anatomical position and functions, extremely liable to become affected by **septic irritants.** These may be either the toxins of bacteria or other organisms, or the organisms themselves; and, in many cases, both these factors are at work. Such irritant material may be carried to the glands either by the

lymph- or by the **blood-stream**; and, in each of these instances, the lesions may differ somewhat, according to the distribution of the lymphatics and of the blood-vessels. Thus, irritants brought by the latter will act first upon the **lymphoid follicles** of which there may be hyperæmia, swelling and softening; whilst the sinus-system may be most affected where there is lymphatic infection. Bacteria reaching the glands in the latter way, tend first to infect the surface plexus of lymphatics, then the sinuses of the cortex and of the medulla, and, lastly, the lymphoid tissue. In the majority of infections, however, all the structural elements of the glands are usually affected together, though often in varying degree.

In **Acute Lymphadenitis,** whether due to soluble toxins or to organisms, there is usually distinct, and sometimes very marked, **swelling** of the glands—varying considerably, however, according to the nature of the irritant. There is usually **softening,** sometimes considerable, and, in extreme cases, **necrosis** of the gland-tissue. In the earlier stages of the inflammation, there is at first, **hyperæmia,** shewing as small points of congestion corresponding to the lymph-follicular cords, but later becoming more diffuse and presenting a pale rose-pink tint, which, however, may rapidly pass off —e. g. in a few hours—as the gland-tissue becomes swollen and packed with cells. **Fibrin** is often present in considerable amount. In intense cases, **hæmorrhages** may occur. These may be punctiform: or, in some instances, diffuse—e. g. in the bronchial glands in woolsorters' disease. Where hæmorrhages do not occur, the colour of the inflamed glands rapidly becomes paler, and then of a whitish or yellowish-white tint, the whole gland structure becoming **crowded with cells**—lymphocytes, proliferated cells from the endothelial and perithelial coats of the lymphatics, and polymorphonuclear leucocytes. In some cases, the **causal organism** may be found, e. g. B. typhosus in the mesenteric and other glands in typhoid fever, Staphylococci, Streptococci, B. anthracis, etc.; but, frequently, such organisms rapidly disappear as a result of phagocytosis. In **bubonic plague,** enormous numbers of B. pestis may be seen closely packed and completely filling the lymph-sinuses, and can be obtained during life by puncture of the infected glands. One or more groups of these enlarged glands or buboes may be found, occurring first, as a rule, in the groin, or, less frequently, in the axilla or elsewhere, according to the original site of inoculation. The intense inflammatory reaction and swelling is usually hæmorrhagic in character, and spreads to the surrounding tissues, matting the glands together. Necrotic softening may supervene, in which case the causal bacteria diminish in numbers and may be difficult to find. In **soft sore** or **soft chancre,** buboes often occur in the inguinal glands, and Ducrey's bacillus, with or without superadded pyogenetic bacteria, may be obtained by gland-puncture.

The inflammatory process may **spread to the periglandular tissues,** and neighbouring glands may become matted together by an œdematous and gelatinous-like inflammatory material.

Where the inflammation has not been too severe, it may gradually

pass off; but there is usually left some degree of enlargement and induration; and, especially if there have been repeated acute attacks, a chronic fibroid condition, with atrophy of the lymphoid cells, usually supervenes.

The presence of pyogenetic bacteria may lead to **suppuration,** commencing as minute purulent foci, which may become confluent and lead to the formation of an **abscess,** confined to one, or to a fused group of glands : or spreading to the periglandular tissues, and, if on the surface or near a cavity, usually rupturing and discharging its contents.

Chronic Lymphadenitis may be due to long-continued **irritation.** Apart from **tuberculosis** and **syphilis,** it may result from **recurrent acute attacks ;** or it may be due to the presence of **pigment** (see above), e. g. carbon-particles in the case of the bronchial glands. The lesion, in such cases is practically always a chronic **fibrosis** with atrophy of the cellular elements. Where **calcification** occurs, chronic tuberculosis is the commonest antecedent lesion.

LYMPHATIC TUBERCULOSIS :—

TUBERCULOSIS OF SEROUS MEMBRANES. (See under **Pericardium, Pleura, Peritoneum,** etc.)

TUBERCULOSIS OF LYMPHATIC VESSELS has already been described (see p. 629).

TUBERCULOSIS OF LYMPHATIC GLANDS.—This condition of lymphatic glands may be **acute** or **chronic,** and infection may occur either by way of **lymphatics** or of **blood-vessels**—very much more commonly by the former of these channels. In some instances, the tuberculosis of the lymphatic glands is **primary.** Thus, the mesenteric glands may be infected by tubercle bacilli which pass directly through the intestinal mucous membrane into the afferent lymphatic channels or lacteals, and so find their way to the glands; or the cervical glands may be similarly infected by organisms which pass through the tonsils, pharyngeal mucous membrane, etc. Frequently, however, some catarrhal inflammation may be present and aid the entrance of the bacilli through the mucous membrane, e. g. of the intestine. In the case of the tonsil and pharyngeal lymphoid tissue, actual tuberculosis of these structures, with formation of giant-cell systems, is common, and, a certain proportion of cases of supposed primary tuberculosis of cervical glands, is undoubtedly due to secondary infection from the primary tuberculous lesions in these tissues.

Secondary infection of lymphatic glands, due to the spread of the bacilli from some other focus of disease, is extremely common, for example in the case of the bronchial and other mediastinal glands in tuberculous disease of the lungs; though, in this connection, it should be mentioned that the lung-tissue itself is very frequently infected by way of the cervical, mediastinal, and bronchial glands, the entrance of the bacilli being effected by the mouth, nose, or ear—perhaps most frequently from carious teeth or by way of the tonsils. Such infections are commonest in childhood and in early adult life, but may be found at almost any
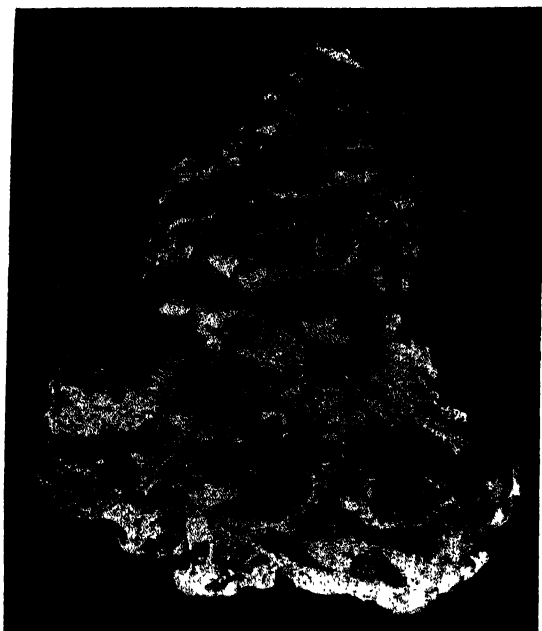
FIG. 284.—Mass of Tuberculous Cervical Glands from a case simulating Hodgkin's disease.

FIG. 285.—Tuberculosis of Mesenteric Glands in child (Tabes mesenterica).

age. The glands at the brim of the pelvis, especially towards the right
iliac fossa, are often affected in young adults, infection occurring probably
by way of the cæcum or commencement of the ascending colon.   Infection
of the mesenteric glands—**tabes mesenterica**—has already been mentioned,
and occurs especially in childhood, the chain of glands at the ileo-cæcal
junction being particularly liable to infection, though any or all the
mesenteric glands may be affected; and, from them, the disease may

Fig. 286.—Tuberculosis of Retroperitoneal Lymphatic Glands around
Abdominal Aorta (from same case as fig. 284).

spread to the retroperitoneal and other abdominal groups, and to the
mediastinal and bronchial glands, etc.

Tuberculosis of lymphatic glands may remain localised for a very
long period, and gradual spontaneous recovery may take place; but,
more commonly, the condition produces **secondary infection of other
glands,** and leads to more wide-spread tuberculosis.   Such extension
may be either acute or chronic, and, in the latter case, it may be very
gradual.

Before the discovery of *B. tuberculosis*, it was difficult to classify
many of the markedly diverse types of glandular lesion which are now

known to be produced by it. In any given case, **two sets of processes may be** observed in the tuberculous lesions, (1) **destructive changes produced by the bacilli,** e. g. caseation, softening, etc.: and (2) **reparative changes on the part of the tissues,** mostly of the nature of cellular proliferation and fibrous-tissue overgrowth, by means of which an attempt is made to localise or isolate the bacilli. These changes vary in degree, the variation being dependent on the resistance of the individual and on the general characters of the bacilli. The more acute and virulent the action of the bacilli and their toxins, the more wide-spread the necrosis and caseation, especially if the resisting power of the tissues is feeble; whereas, if resistance is good and the action of the bacilli weaker, overgrowth of the tissues of the gland occurs around the lesion.

The following types of tuberculous lesion in glands may be distinguished :—

1. **Giant-cell systems,** with the usual epi- or, more accurately, endothelioid and lymphocyte-like cells around them. This form may be either **acute** or **chronic,** and is well seen in the bronchial glands in cases of phthisis. The affected glands may shew little change to the naked eye; or minute, white, or greyish-white, nodules, best seen in pigmented glands, may be present, the intervening gland-tissue often presenting a congested pinkish appearance. Such glands may gradually become fibrous, with the occurrence of little or no caseation.

2. In other instances, glands may undergo rapid **caseation.** The minute multiple areas, first observed, enlarge, coalesce, and come to present a whitish or yellowish-white appearance like the cut surface of a potato or cheese. This condition may spread throughout the whole, or a large part, of the gland; and, when this is the case, it is not uncommon to find necrotic softening and an abscess-like condition supervening; or the caseous material, contained within the thickened fibrous-tissue capsule of the gland, may, in whole or in part, become infiltrated with lime-salts and become of stony hardness—a condition most frequently seen in the bronchial or mesenteric glands.

3. In some cases, the lymphatic glands may become **enlarged,** with **great proliferation of the endothelial cells of the lymph-sinuses.** These cells separate off and become rounded, and may be found in great numbers in the sinuses, causing compression-atrophy of the lymph-follicular cords, which do not become proliferated. This condition, before its tuberculous nature was recognised, was described as " large-celled hyperplasia " of lymphatic glands, a somewhat similar change occurring also in syphilis. Sometimes no giant-celled systems can be found in such glands, and it may be difficult to differentiate them from other chronic inflammatory conditions. Moreover, a certain degree of this type of reaction may be produced by the **toxins** alone, apart from the presence of the bacillus itself in the gland. Glands shewing tuberculosis of this chronic hyper-type may, later, undergo caseation and calcification, the endothelial becoming swollen, granular, and necrotic, and fusing to form a

homogeneous caseous mass. This form of tuberculosis is often found in the bronchial and mesenteric glands; and it is also seen in certain cases where wide-spread enlargement of practically all.the lymphatic glands of the body·occurs. In these cases, the glands may form large tumour-like masses, *e. g.* in the neck, axilla, mediastinum, abdomen, etc., closely resembling the condition found in Hodgkin's disease, from which it is sometimes difficult to differentiate this form of tuberculosis clinically *(see figs. 284, 286, and 288).*

Tubercle bacilli may be found microscopically in tuberculous glands. In some of the acute caseating forms, they may be present in great numbers; but, in many cases, especially in the variety last described, none—at all

Fig. 287.—Lymphatic Gland, shewing tubercle-follicles with caseation and giant-cell formation.   ×50.

events in the form of acid-proof [1] bacilli—may be found microscopically; though their presence in an infective form may be demonstrated by inoculation into a susceptible animal such as a guinea-pig. Full discussion of the **types of the tubercle bacillus** causing glandular infection must be left to the special books on Bacteriology. It is sufficient here to mention that work by Mitchell [2] and others has proved that, in a very large proportion (in some areas as many as 90 per cent. of cases

[1] Investigations by Much seem to shew the probability of the existence of certain infective forms of the tubercle bacillus other than the well-recognised acid-proof form. Much describes, in addition to (*a*) the ordinary acid-proof bacillus stainable by the Ziehl-Neelsen method, (*b*) a non-acid-proof bacillary form, often shewing well-marked granules, and (*c*) free non-acid-proof granules. The latter two forms can be stained by a modified Gram's method.

[2] Mitchell, "The Infection of Children with the Bovine Tubercle Bacillus," *Brit. Med. Jour.*, January 17. 1914.

of tuberculous adenitis in infants and children) the infection is produced by the **bovine type** of bacillus.

Waxy or **amyloid disease** may occur in the glands in chronic tuberculosis.

SYPHILITIC LYMPHADENITIS.—The glands into which the lymphatics draining the area of the **primary sore** open, become enlarged and hard, the changes being inflammatory in character. In the sore and in the enlarged inguinal glands, the spirochætes may be found in large numbers, and their demonstration will prove the case to be syphilis at a very early stage—a fact of great diagnostic value in early doubtful cases before the establishment of a positive Wassermann Reaction in the blood. Suppuration may be superadded from secondary infection with pyogenetic cocci. During the **secondary stage** of the disease, a wide-spread enlargement of lymphatic glands may occur, characterised by proliferation of the endothelial cells of the sinuses and thickening of the reticulum. **Gummata** may form in the glands, but are somewhat uncommon. Occasionally, in congenital cases of syphilis and in late secondary infection, glandular enlargement may be so marked as to simulate Hodgkin's disease.[1]

Syphilis is an important cause of **waxy disease** in glands, as in other organs and tissues.

HODGKIN'S DISEASE, or LYMPHADENOMA.—That this disease constitutes a distinct pathological entity has been denied by many; whilst, in the literature of the subject, several distinct conditions, some of which have been referred to on p. 631, have been erroneously described under this name. When these are excluded, there remains, however, a definite group of cases, the characteristics of which are sufficiently distinctive to warrant their classification under the term **Hodgkin's disease** or **lymphadenoma.**

In a typical case, there occurs a **progressive enlargement of the lymphatic glands,** usually beginning in the cervical, or, less commonly, in the inguinal, axillary, or some other group. This enlargement may commence on one side, spread progressively to the opposite side, and to the other lymphatic glands and lymphoid tissues of the body, though, in certain cases, the condition may remain localised in one set of glands for a long time. The **thymus** may occasionally be the primary seat (Ribbert). At some period of the disease, varying in individual cases, though sometimes comparatively late in its course, the **spleen** becomes affected. Mild irregular **pyrexia** is usually a feature of the disease. In the earlier stages, the **blood** may shew comparatively little alteration, but, as the disease advances, a progressive type of **secondary anæmia** is established. The **erythrocytes** may shew a moderate reduction in their number, but seldom

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[1] Discussion on Enlargement of Cervical Lymphatic Glands in Syphilis. H. C. Cameron, F. J. Poynton and F. Parkes Weber. *Proceedings of Royal Society of Medicine.* Section of Children's Diseases. Vol. XIII. No. 2, p. 7, December 1919

fall below 2,000,000 per c.mm. Nucleated red cells are not commonly found. The **hæmoglobin** is usually considerably reduced in amount. Variations in the numbers of the **white cells** are not especially characteristic. In some instances they are distinctly diminished, but many cases have been reported in which they have been increased. Eosinophilia has been described in several cases. The lymphocytes may shew slight relative increase, in cases where the indurative changes in the glands and spleen are not so pronounced as usual. Marked polymorphonuclear leucocytosis may supervene from the presence of secondary complications, a fact which probably explains why some cases of Hodgkin's disease have been regarded as undergoing leukæmic transformation. Periods of quiescence, or even spontaneous diminution in the size of the enlarged glands, may occur during the course of the disease, especially as a terminal phenomenon in some cases; but, as a rule, the condition is a progressive one, practically always leading to a fatal termination. Death may supervene from asthenia, or from pressure of the enlarged glands upon some important structure, for example the trachea or bronchi, lungs, heart, bile-duct, or some of the great vessels or nerves. From the same cause, paralysis, dropsy, and other phenomena may occur. There appears to be little tendency to the occurrence of hæmorrhages.

Ætiology.—Practically nothing is known of the ultimate cause of the disease. Males are more commonly attacked than females, and it is during adolescence and early adult life that the majority of cases occur. Although the condition in some ways resembles tumour-formation, it has closer analogies with certain chronic infective processes, especially those seen in tuberculosis and syphilis, and it appears not unlikely that it may ultimately be found to be caused by some, as yet unknown, infective agent. The disease does not appear to be due to *Bacillus tuberculosis*, as has been alleged by some observers; and experimental inoculation into animals of material from uncomplicated cases has failed to demonstrate the presence of this organism, and, in such cases, the tuberculin-test has also proved negative (Reed). Tuberculosis, however, is not an uncommon **complication** of the disease. Various observers have described the occurrence of spirochætes, or the growth of diphtheroid and other organisms from the glands in Hodgkin's disease, and special attention has been directed to the occurrence of one diphtheroid (*Corynebacterium granulomatis maligni* of Negri and Miermet) as a possible ætiological factor. The evidence, however, of the relationship of any of these organisms to the disease is very inconclusive, Cunningham, of the Roosevelt Hospital, New York, considering the diphtheroid bacillus to be a laboratory contamination. Billings and Rosenow state that they have isolated an organism from twelve cases, and have treated these with vaccines made from the cultures, apparently with some success. Their results, however, await further confirmation. Meantime, the true ætiology of the disease must be regarded as still unknown.

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Morbid Anatomy.[1]—Though the disease may remain localised· for a varying period—by the time death supervenes, the **lymphatic glands** throughout the body, especially in the positions already mentioned, are usually greatly enlarged, and form considerable tumour-like masses, the individual glands being often as large as a pigeon's or a hen's egg. Unless matted together by secondary inflammatory adhesions, they remain more or less discrete, being held together by loose connective tissue, which can be easily separated. There is usually no tendency to infiltrate the surrounding parts, though such infiltration has been described in exceptional cases. The individual glands vary somewhat in consistence. In some cases—especially in the earlier and more acute forms—they are soft; but, more commonly, especially where the disease has lasted some time, they are indurated, firm, and elastic. It is not uncommon to find softer and more indurated glands side by side in the same case. **On section,** they may shew a pale pinkish tint, especially in the more acute cases, or very commonly, as the disease becomes more chronic, a semi-translucent greyish appearance, often with bands of a more opaque yellowish colour running through them. Sometimes, the whole gland may exhibit this opaque yellowish appearance. Occasionally, small areas of caseation, simulating tuberculosis, may be present, and microscopical

FIG. 288.—Hodgkin's Disease or Lymphadenoma. Large tumour-like mass of lymphatic glands from axilla.

examination may be necessary to distinguish between the two conditions. **Microscopically,** the earliest stage of the process is seen as a **hyperplasia of the lymphoid tissue,** but upon this there rapidly supervene **proliferation of the reticular and endothelial cells, and a progressive increase of the reticulum itself,** leading to **fibrosis** of the gland-tissue and disappearance

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[1] An excellent account of the morbid anatomy and histology of Lymphadenoma, is given by Stuart McDonald, in the *Transactions of the Newcastle-upon-Tyne Clinical Society* for December 1910.

of the lymphoid cells. Increase in the number of **eosinophil cells** in the earlier and more acute stages is of frequent occurrence, but a more constant and characteristic phenomenon is the presence of **phagocytic giant-cells,** both **mono-** and **multi-nucleated,** apparently derived from endothelial or reticular cells. Large phagocytic syncytial masses may also be found. In the later stages, the cellular elements are practically entirely replaced by fibrous tissue, and the structure comes to resemble that of dense, scar-tissue.

Spleen.—The condition of this organ is extremely variable. In some cases, it is only slightly enlarged, whilst in others it may be moderately, or even greatly, increased in size. The natural shape is usually well preserved, and the organ is firm in consistence. **On section,** to the naked

Fig. 289.—Spleen in Hodgkin's Disease. Malpighian body in process of fibrous oblitera-
tion, and surrounded by a ring of pigmented phagocytic cells.   ×75.

eye, there may appear to be merely a congestive condition present; but, again, there may be found characteristic, scattered, whitish or yellowish-white, suet-like masses, which are usually distributed along the lines of the larger arteries. In the earlier and more acute cases, their colour is usually greyish-pink. These areas may be more or less diffuse, apparently spreading into the organ from the hilus, along the lymphoid sheaths around the arteries. In other cases, these areas are more irregularly scattered, and form isolated, rounded, or irregularly-shaped masses, which may be as large as a bean or a cherry. These pale, whitish masses consist of altered peri-arterial lymphoid sheaths—i. e. the so-called Malpighian bodies—which have undergone a process similar to that already described as occurring in the lymphatic glands, namely (following, it may be, a preliminary and temporary hyperplasia of the lymphoid tissue proper), proliferation of the endothelial plates and reticulum, and a corresponding

diminution of the contained lymphocytes. The process tends to spread into the surrounding areas of pulp, which thus become in part fibrosed. Where the condition is spreading, the proliferated endothelial and reticular cells, and giant-cells formed from these, are actively phagocytic towards red blood-corpuscles, and usually contain large quantities of blood-pigment, producing around the periphery of the nodules a brownish zone, which can often be distinguished with the naked eye.

The changes in the **bone-marrow** are somewhat variable, and have not yet been fully investigated. Longcope [1] describes a leucoblastic reaction characterised by the presence of " myelocytes and large lymphocytes," the most remarkable deviation from the normal consisting of a great excess of eosinophil leucocytes and myelocytes. Suet-like nodules like those occurring in the other organs were not observed by this writer, but have been described by several authors. These nodules shew the same reticular proliferation, etc., already described as occurring in the lymphatic glands and spleen.

Similar nodules are frequently found in the **liver** in such cases, usually combined with some degree of cirrhosis and fatty degeneration. These nodules occur in the connective tissue of the portal tracts as lymphoid areas, which, later, undergo reticular proliferation, giant-cell formation, and then fibroid transformation. They are likewise occasionally seen in the kidneys, lungs, and even in the skin (Greenfield). In the last-mentioned tissue, the lesions may be (1) a true lympho-granuloma cutis, the nodules having the typical lymphadenomatous structure; or (2) a group of lesions set up by the general infection, but not shewing the characteristic lesion locally (Cole). The lymphoid tissue of the intestines —Peyer's patches and solitary follicles—and of the stomach may also become involved, and may, in rare cases, undergo ulceration.

Longcope,[2] in his paper on the subject, comes to the following conclusions :—

1. Hodgkin's disease should be considered as a distinct clinical and pathological entity.

2. The lesions in the lymph-glands and other organs are especially characterised by the early increase in the lymphadenoid tissue, with later proliferation of endothelioid cells, formation of uninuclear and multinuclear giant-cells, thickening of the reticulum, and final overgrowth of connective tissue. Eosinophils, though not specific, are frequently found in great abundance. Together with the abundance of eosinophils in the lymph-glands, the eosinophilic leucocytes and myelocytes of the bone-marrow are increased.

3. The process originates in lymphoid tissue, and, during the course of the disease, new lymph-glands are constantly being formed, which ultimately become the seat of the lymphomatous (lymphadenomatous) growths.

4. In rare instances, the retroperitoneal lymph-glands may be the only group affected.

[1] Longcope, " On the Pathological Histology of Hodgkin's Disease, with a Report of a Series of Cases," *Bulletin of the Ayer Clinical Laboratory*, Philadelphia, U.S.A., 1903, No. 1, p. 4.
[2] Longcope, *loc. cit.*

5. The ætiology of Hodgkin's disease is so far unknown. The tubercle bacillus plays no part in the production of the lesions.

TUMOURS of LYMPHATIC GLANDS and of lymphoid tissue generally. These present many difficulties in their classification, and in their differentiation from hyperplasias and other changes in certain so-called blood-diseases, and from chronic inflammatory and infective enlargements. The following types of **primary new growth** may be distinguished.

Fig. 290.—Lymphatic Gland, shewing malignant infiltration with squamous-celled carcinoma. × 60.

Lymphoma.—Tumours precisely resembling proliferated lymphadenoid tissue, in which the lymphocytes, endothelial cells, and reticulum appear in practically their normal proportions, may occur. These are seen in the **mediastinum,** where they may arise from ordinary lymphatic glands, or from the thymus gland. In the latter case, they may reproduce the structure of the thymus, and even the Hassal's corpuscles may be found in the tumour. Lymphomas may also arise in the **tonsils,** and in the **cervical, abdominal, and other lymphatic glands.** They have been described as occurring in the **kidney,** and in the **lymphatic glands** about the head of the pancreas and near the hilus of the liver. Such tumours may remain apparently non-malignant, but, in some cases, there may be

a tendency to the secondary infection of other lymph-glands and lymphoid structures, e. g. Peyer's patches and the solitary lymphoid follicles of the intestine. These may ulcerate, forming the so-called **lymphomatous ulcers.**

Lympho-Sarcoma.—In this extremely malignant form of tumour, there is enormous increase in the number of lymphocytes or lymphocyte-like cells, with no corresponding increase of endothelial plates and reticulum, both of which structures remain extremely scanty. Such tumours arise most frequently from **mediastinal** and **retro-peritoneal**
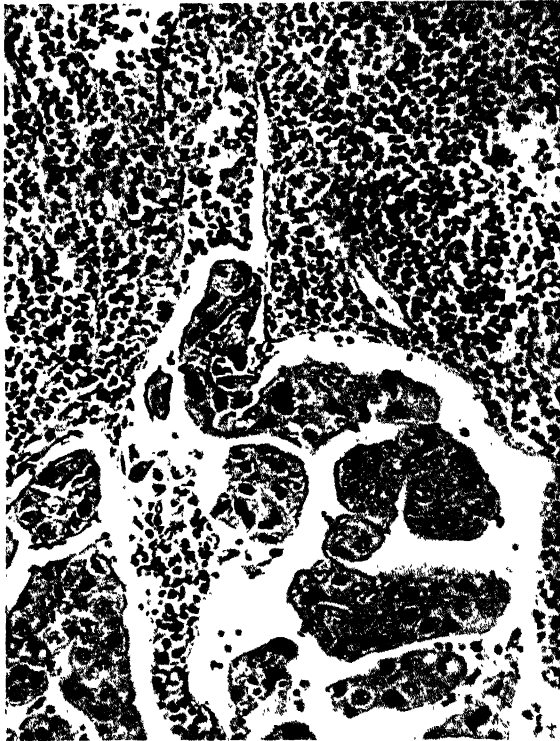
Fig. 291.—Axillary Lymphatic Gland, shewing secondary invasion with cells of scirrhus cancer of breast. × 200.

lymphatic glands, but they may originate also from lymphoid tissue around the intra-pulmonary bronchi, and elsewhere. The enlargement of lymphatic glands in the leucocythæmias and analogous conditions is dealt with on p. 611.

Secondary growths of malignant epithelial tumours in glands are extremely common, for example, implication of the cervical glands in squamous epithelioma of the tongue : of the axillary and other groups of glands in scirrhus and other malignant tumours of the mammary gland : of the mesenteric and retro-peritoneal glands in gastro-intestinal cancers, etc., etc. Secondary growths of sarcomas are also by no means un-common—though sometimes stated to be so.

LYMPHATISM or STATUS LYMPHATICUS

Though comparatively rare, this condition is one of considerable importance, owing to the liability of those who suffer from it—most commonly children or young adults—to **sudden death** from apparently trivial causes, such as a sudden shock or fright, or on the administration of an anæsthetic such as chloroform or ether. The presence of the condition has, in many such cases, been quite unsuspected during life, and may be revealed for the first time by the **post-mortem** examination. There is **general hyperplasia of the lymphoid tissue throughout the body.** The lymphatic glands, especially those in the mediastinum and abdomen, are enlarged, as are also the tonsils and pharyngeal adenoid tissue, thymus, and spleen, and the Peyer's patches and other adenoid tissue in the intestine, the solitary follicles of the large intestine being specially prominent. The posterior portion of the dorsum of the tongue is often unusually rough, especially in the neighbourhood of the circumvallate papillæ, which may be themselves distinctly hypertrophied. The thymus enlargement is frequently very marked, and to pressure by it upon the trachea the fatal issue in some cases of lymphatism has been attributed. In the majority of cases, this is certainly not the true explanation, and most authorities now believe that some toxic material is elaborated and poured into the system from the enlarged glands—the condition of so-called " **lympho-toxæmia.**" Hyperplasia of the bone-marrow (fatty, being replaced by red marrow), and of the thyroid gland, is recorded in some cases, as is also an under-development or hypoplasia of the heart and great vessels. Areas of " small-celled infiltration " and other inflammatory and degenerative changes have been described as occurring in the myocardium. The cause of the condition is unknown.

HÆMOLYMPH GLANDS

These closely resemble ordinary lymphatic glands in structure, the chief point of difference being the presence of blood in the sinus-systems between the lymphoid follicles. Little is yet known of their physiology and pathology, but marked enlargement of them has been observed in some " blood-diseases " such as **pernicious anæmia, splenic anæmia,** etc., and also in **exophthalmic goître** (*q. v.*, p. 840), and certain other conditions. The glands are specially found in the abdomen, *e. g.* about the brim of the pelvis, and along the aorta and inferior vena cava, iliacs, splenic vessels, etc. Marked phagocytic activity towards red blood-corpuscles, on the part of the endothelial cells of the sinuses, is usually to be observed in these glands, especially in the diseases just mentioned.

DISEASES OF THE SPLEEN

THE **Spleen** is an organ which is not necessary to life (*see under* **Splenectomy,** p. 660), and all its functions are not yet fully determined. Amongst other activities, it appears to act as a filter for the blood which passes through it, and serves to sift out damaged and effete blood-corpuscles, as well as bacteria and other organisms. Active phagocytosis on the part of the endothelial cells of the pulp proceeds in·health, and may occur to a very exaggerated degree in disease. Various processes carried out by ferments or enzymes occur in the organ, but are, as yet, only imperfectly understood. Certain of these processes appear to have a special bearing on the production of immunity, in some of its aspects at all events; and it reacts very readily in toxic diseases. Its anatomical relations to the portal circulation are important; and, by the rhythmic contractions of which it is capable, owing to the presence of non-striped muscular fibres in its capsule and trabeculæ, it probably aids the flow of blood through the liver. The spleen is therefore, specially affected by diseases which interfere with the hepatic circulation.

The organ can now no longer be regarded as a producer of red blood-corpuscles, except during intra-uterine life. Similarly, after birth, polymorphonuclear leucocytes are produced solely in the bone-marrow, and not in the spleen, the only hæmopoietic functions of which appear to be the formation of lymphocytes in the Malpighian bodies or lymphadenoid sheaths developed around the smaller arteries of the organ : and also, in all probability, the production of certain of the large mononuclear cells of the blood, some, at all events, of which appear to arise from endothelial cells—a type of cell in which the spleen is extremely rich. Reference has already been made to the hæmolytic activities of the organ (*see also* pp. 597, 608–9, 613, 622, etc.).

MALFORMATIONS and MALPOSITIONS.—Accessory spleens, usually small in size (**Spleniculi or Splenunculi,**) are of very common occurrence. They generally vary from the size of a pea up to that of a cherry, and are more or less spherical in shape. As a rule, such accessory spleniculi are few in number—most commonly only one is found—and are usually situated near the hilus of the main organ. More rarely, they may be multiple, and may be situated elsewhere, *e.g.* in the mesentery, etc. They almost always participate in pathological enlargements and other abnormalities of the main gland.

Movable or Wandering Spleen.—Owing to laxity of its ligaments in some cases, the organ may be unduly, and even freely, movable. Twisting

of the pedicle and constriction of the contained vessels may lead to interference with its blood-supply, and perhaps to necrosis.

INJURIES OF THE SPLEEN may occur even in health, *e. g.* from severe crushing injuries to the trunk; but rupture occurs much more readily if the organ is **previously diseased,** and especially if it is enlarged, *e. g.* from malaria, when a very slight accident may cause rupture. In crushing injuries, the spleen is usually folded upon itself, and ruptures on its outer or convex surface, an occurrence which generally leads to extensive, and perhaps fatal, hæmorrhage. Exploratory puncture may also give rise to serious hæmorrhage, especially if laceration from respiratory or other muscular movements occurs.

CHANGES RELATED TO THE SURFACE AND PERITONEAL INVESTMENT OF THE SPLEEN.—Local peritonitic inflammation and thickening, often producing adhesions to neighbouring structures, especially to the diaphragm, are very common. Localised chronic inflammatory changes in the capsule may sometimes attain a considerable thickness, leading to the formation of dense, white areas of fibrous tissue almost "cartilaginous" in consistence. A "wandering" or "floating" spleen may become adherent in some abnormal position in the abdomen. When the spleen becomes enlarged, *e. g.* in leukæmia, the enlargement usually occurs downwards, forwards, and inwards. Occasionally, this may be prevented by old adhesions or by the presence of an exaggerated development of a peritoneal shelf, formed by the costo-colic ligament, under its lower pole.

ATROPHIC CHANGES IN THE SPLEEN.—Atrophy of the spleen occurs normally as a **senile** change, the Malpighian bodies, in common with lymphoid structures in other parts of the body, becoming progressively less active and undergoing atrophic changes with advancing age. The pulp also becomes diminished in bulk, mainly from atrophy of its cells; and the fibrous tissue, especially of the trabeculæ, is relatively increased in amount. The capsule of the organ becomes wrinkled, and the weight of the spleen may fall as low as 2 or $2\frac{1}{2}$ ounces (60–75 grms.). **On section,** the tissue has a dull brownish-red colour, the Malpighian bodies being inconspicuous, and the trabeculæ showing as pale, ragged, fibrous threads, standing out somewhat above the general level of the cut surface. The consistence of the organ varies, but, most frequently, it is tough, dry, and soft, rather resembling a piece of flabby muscle to the touch.

The majority of pathological changes in the spleen are, however, associated with **enlargement** of the organ.

WAXY or AMYLOID DEGENERATION.—This disease may affect the spleen in one of two ways, which, according to the anatomical distribution of the change, are respectively known as **sago-waxy,** and **diffuse waxy,** degeneration of the spleen. In some cases, a **combination of these types** may be found in the organ.

The **Sago-waxy Type** is much the commoner of the two. The spleen is usually moderately enlarged, perhaps to twice its normal bulk, but,

in many cases, there may be little increase, and even some diminution, in the size of the órgan. In consistence it is firm, its cut margins remaining sharp, and its natural shape being well maintained. **On section,** the surface is seen to be studded over with great numbers of small, rounded or slightly irregular, clear glistening white or colourless, translucent areas, usually about the size of a pin's-head or a little larger—*i.e.* a couple of millimetres or so in diameter—and very much resembling grains of boiled tapioca or sago in appearance. On the application of iodine to the cut surface, these points are stained a deep mahogany-brown colour (*see* fig. 292). The intervening pulp-tissue is usually dark red in colour from **chronic venous congestion,** which is very often associated with

Fig. 292.—Waxy or Amyloid Degeneration of Spleen. " Sago-waxy " type. (Lower portions treated with iodine.)

waxy disease, both on account of general systemic venous engorgement, and more especially from portal stagnation due to associated disease of the liver. **On microscopical examination,** in an unstained section, the waxy material has a bright, clear, transparent, glassy appearance with **transmitted,** and a black, structureless appearance with **reflected,** light. In sections stained with iodine, (*see* Plate II, fig. 1), or with methyl violet, these rounded waxy areas shew the typical staining reactions of amyloid material (*see* pp. 59–60), and are seen to correspond with enlarged Malpighian bodies. The central arteriole of these usually, but not always, shews waxy disease. The main change is in **the adenoid reticulum and in the perithelial connective tissue of the capillaries of the Malpighian bodies,** the affected tissue-elements being greatly swollen, and presenting a structureless, homogeneous appearance, **the intervening lymphocytes and other cellular elements undergoing pressure-atrophy and disappearing.** A small area of lymphoid tissue immediately around the central arteriole frequently remains comparatively unaffected until late in the disease, and, in this zone, the lymphocytes may survive, though usually in much diminished numbers. The **arterioles of the pulp** generally shew distinct waxy change; and the adenoid reticulum of the pulp—except immediately around the Malpighian bodies, from which the disease may shew direct local extension outwards into the pulp—is either unaffected, or shews only a few streaks of waxy degeneration here and there. The venous sinuses of the pulp usually shew associated chronic venous congestion, leading to extensive

compression-atrophy of the pulp-cells. The waxy change in the arterioles, etc., follows the usual method of distribution of the disease (see p. 62).

Diffuse Waxy Disease of the Spleen.—In this form, which is more especially associated with syphilis—though it may also be found in chronic tuberculosis—there is extensive affection of the splenic pulp. The enlargement of the organ is usually rather more pronounced than in the sago-waxy type, the organ being extremely **firm** and resembling hard india-rubber in consistence. The cut surface has a more or less homogeneous, semi-translucent appearance, often with a pale pinkish-red tint. The Malpighian bodies are widely separated and minute, and may be almost, or even quite, invisible to the naked eye. With iodine, a uniform deep mahogany-brown coloration is obtained (fig. 293). **On microscopical examination,** the waxy change is found implicating the **supporting reticulum** and **the perithelial connective tissue of the venous sinuses of the pulp,** which are thus sharply outlined by the change, and, if also distended by chronic venous congestion, produce a characteristic fenestrated appearance of the tissue (see Plate II, fig. 2). The endothelial cells lining the venous sinuses do **not** undergo the waxy change. The **pulp-cells are compressed and usually shew extensive atrophy.** The **arterioles,** both of the pulp and of the Malpighian bodies, shew waxy degeneration of their connective tissue. The **Malpighian bodies** are widely separated by the enlarged pulp. They are small and compressed, and may shew a spread of the waxy change inwards from their periphery; though, in some cases, they are unaffected by the disease.

Fig. 293.—Diffuse Waxy Degeneration of Spleen. (Lower portion treated with iodine.)

HYALINE DEGENERATION occurs in the **vessels** of the spleen, especially in the **arterioles,** in some of the **acute infective fevers,** most commonly in diphtheria and scarlet fever (see Plate II, fig. 6). It is an **acute toxic change,** and is usually associated with acute congestion of the organ. A more **chronic form** of the degeneration is frequently found in **Bright's disease.** Hyaline degeneration may be followed by calcification of the affected areas in the vessel-wall.

PIGMENTATION AND PHAGOCYTOSIS IN THE SPLEEN.—Owing to the **hæmolytic activities** of the spleen, the presence of a certain amount of **blood-derived pigment** is a normal phenomenon, most of the pigment being contained within the phagocytic endothelial cells of the pulp. In any condition characterised by **increased blood-destruction,** notably in the **anæmias,** both primary and secondary, and in **acute and chronic**

septicæmias and toxæmias, the hæmolytic activities of the organ are increased, and, consequently, the phagocytic cells and their contained pigment are in greater evidence (*cf.* Plate III, fig. 2). Good examples of such processes are to be seen in the spleen in the case of **pernicious anæmia,** the toxæmia of **diphtheria,** or in **chronic malaria,** though marked degrees of the change may be found in almost any analogous condition. The endothelial cells proliferate, and, in some instances, enlarge to form multinucleated plasmodial- or giant-cells resembling a similar type of cell found under like circumstances in the bone-marrow (*see* Plate XIV, fig. 4). These phagocytic cells, which may shew large numbers of cell-inclusions— mostly red blood-corpuscles (which, in the case of malaria, may contain the malarial parasite)—may be seen in sections, but are best studied in films fixed while still wet with a saturated solution of corrosive sublimate in saline. They may attain an enormous size in pernicious anæmia, and also notably in splenic anæmia. The naked-eye evidence of such hæmolysis is seen as a distinct brownish tint of the splenic pulp. The pigment, though it may contain iron, *e.g.* in the case of pernicious anæmia, often does not give a definite Prussian-blue reaction, probably on account of the iron being in somewhat firm union with organic material- the application of potassium ferrocyanide and hydrochloric acid, in many cases, producing a variable greenish- or bluish-black discoloration.

Post-mortem discoloration or **pseudomelanosis**—generally of a dark greenish- or violet-black tint—is extremely common, especially on the lower part of the organ where it is in contact with the intestine. Such *post-mortem* discoloration is due to the action of sulphuretted hydrogen upon the iron of the blood or blood-pigment. It may be localised to the surface, or may penetrate the substance of the organ for a varying distance.

VASCULAR DERANGEMENTS OF THE SPLEEN :—

(*a*) **ACUTE** or **ACTIVE HYPERÆMIA** will be discussed when dealing with the **Spleen in Acute Diseases** (p. 654).

(*b*) **CHRONIC VENOUS CONGESTION.**—This condition may form part of a general venous engorgement, *e.g.* in diseases of the heart or lungs, in which the inflow of venous blood into the heart is impeded; or it may be produced by obstruction of the portal circulation by disease of the liver, or from tumours or other lesions producing pressure on the portal or splenic veins. The most typical examples of the condition are seen in heart-disease. The organ is usually moderately enlarged, and firm in consistence. It becomes relatively thicker, and especially broader, in proportion to its length, often coming to have a somewhat oblong shape. The notches are generally well preserved (*see* fig. 294). The capsule and trabeculæ are thickened, and the muscular fibres in them may be increased. The pulp has a characteristic dark purple-red colour, and

the Malpighian bodies are widely separated, small, and indistinct, owing to compression by the engorged and dilated venous sinuses of the pulp. The large and medium-sized veins, which can be seen running in the trabeculæ, are dilated. **On microscopical section,** this dilatation can be well seen, together with thickening of the vein-walls and trabeculæ. The pulp is mostly occupied by the **dilated venous sinuses,** the walls of which, lined by endothelium, are abnormally distinct (*see* Plate II, fig. 2, in which, however, waxy degeneration is also present). The intervening pulp-tissue, and also the Malpighian bodies, are atrophied from pressure.

Fig. 294.—Spleen. Chronic Venous Congestion.

There is, usually, a considerable amount of **blood-pigment** within the phago-cytic endothelial cells, and, to a less extent, free in the lymphatic spaces of the pulp.

(c) **INFARCTION OF THE SPLEEN.**—The subject of infarction is fully dealt with on pp. 150 *et seq.*, especially p. 154. Infarcts are of very common occurrence in the spleen, and may be due to **embolism,** *e.g.* in valvular heart-disease, there thus being, usually, an associated chronic venous congestion of the spleen: or to **thrombosis,** which is the probable cause of the infarcts that are of common occurrence in the enlarged spleens of myelogenous leukæmia, splenic anæmia, and analogous diseases. Thrombosis of the main splenic vein produces a condition of infarction of the whole organ.

Infarcts in the spleen may be multiple, and are often of large size. They are found most frequently on the convex outer surface or borders of the spleen, though, when large, they may occupy a horizontal or

transverse zone *through the entire thickness of the organ. Seen on the* outer surface, they may be irregularly rounded, or may form a bar-like area running across the spleen (*see* fig. 295). In the former case, they are usually irregularly wedge-shaped on section, the base of the wedge being towards the free surface. In infarction, the whole spleen may be considerably enlarged—usually more so than in uncomplicated chronic venous congestion—especially where the infarcts are multiple from repeated embolism. All infarcts of the spleen are at first hæmorrhagic and deep red in colour. Later, they become pale, and undergo gradual absorption, total or partial, according to their size. As absorption proceeds, they become surrounded by a capsule of fibrous tissue, which may, later, undergo contraction and lead to the formation of a depressed puckered scar on the surface of the organ (*see* fig. 296). Local peritonitis may occur over the area of infarction, and may give rise to adhesions. Where the causal emboli are septic, *e. g.* in ulcerative endocarditis, or where secondary infection with pyogenetic organisms occurs, the infarcts may soften and break down to form abscesses, which may burst and produce general peritonitis or, if localised by adhesions, may give rise to the condition of peri-splenic abscess.

THE SPLEEN IN ACUTE TOXIC AND SEPTIC DISEASES, *e. g.* **the acute infective fevers.** In such acute conditions, whether it is the toxins or the organisms themselves, or a combination of these, that are present in the circulating blood, the spleen is extremely liable to be affected.

FIG. 295.—Infarct in Spleen, shewing raised surface, transverse arrangement, and pallor.

The so-called **Active Hyperæmia** or **Acute Congestion** of the spleen, in the majority of these diseases, is largely of the nature of a reaction or attempt to antagonise the poison of the disease. **Swelling** of the organ may occur very rapidly—even in a few hours—in intensely acute diseases, *e. g.* in an acute attack of malaria, or in typhus fever, streptococcal septicæmia, etc. This is due partly to **congestion of the pulp** and **swelling of the Malpighian bodies ;** but, later, it is due more especially to **proliferation of endothelial and pulp-cells,** and to the **accumulation of leucocytes** in the tissues of the organ. The nature of the enlargement varies considerably, however, according to the nature of the causal organism or infective agent. Thus, in **typhus fever,** the spleen may be deep red in colour; in **erysipelas** and other **streptococcal infections,** in **pneumonia,** and in **staphylococcal cases,** it is often paler, the **diffluent** pulp having a creamy pinkish-white tint, though the occurrence of **hæmorrhage**

may produce a darker red colour. In such cases, the spleen is so extremely soft that it is very easily ruptured on removing it from the body; and, on section, the pulp can be scraped or washed away with great ease. In some cases, *e. g.* in scarlet fever, the Malpighian bodies may be enlarged as well as the pulp-tissue.

In **typhoid fever,** the spleen may **not** be softened, and the Malpighian bodies may or may not be enlarged the most important change in the organ being the marked proliferation of the endothelial cells lining the sinuses of the pulp.

Apparently the only fever in which **no** swelling of the spleen occurs

Fig. 296.—Old Infarct in Spleen, shewing pale caseous mass surrounded by a fibrous-tissue capsule. Note depression below the surface of the spleen. × 5.

is **yellow fever,** perhaps on account of the amount of blood lost by gastric hæmorrhage.

In **many bacterial diseases,** especially those of septicæmic nature, the **causal organisms** may be found specially aggregated in the spleen, in which they may be demonstrated on microscopical or cultural examination, for example in the case of **typhoid** and **Mediterranean (Malta)** fevers, **staphylo-** and **strepto-coccal septicæmias,** etc.

Actual **suppuration** in the spleen, apart from its occurrence in **ulcerative**

endocarditis and **pyæmia,** is rare. Secondary abscesses may occur in malaria or in typhoid fever. Such abscesses in the spleen tend to occur towards the surface, where they may rupture and, if localised by adhesions, give rise to **perisplenic abscess.**

CHRONIC INTERSTITIAL SPLENITIS.—This is usually an enlargement of the spleen, with induration from proliferation of its fibrous tissue, which may arise from recurring acute attacks, *e. g.* in malaria. The endothelial cells of the pulp usually shew proliferation, and may contain excess of pigment; and the Malpighian bodies may be compressed and atrophied.

TUBERCULOSIS OF THE SPLEEN.—Tuberculous infection of the spleen is always **secondary.** The surface of the organ may be involved in' tuberculous peritonitis, and tuberculous adhesions of the spleen to the surrounding organs and tissues, especially the diaphragm, are common. In **general acute miliary tuberculosis,** numerous small, greyish-white, opaque, nodular areas may be found scattered throughout the substance of the organ and under the capsule. They may be distinguished from the Malpighian bodies, which they closely resemble, by their being somewhat firmer and more prominent, and by their being also found on the surface of the organ. **On microscopical examination,** though they may occur in any part of the spleen-tissues, they are most frequently found along the course of the arteries, and are, therefore, especially seen in the Malpighian bodies. Typical tuberculous **giant-cells** are often present, but the proliferative changes are, as a general rule, not pronounced, whilst caseation is usually a well-marked feature.

Fig. 297.—Caseous Tuberculous Nodules in Spleen.

In a second type of tuberculosis of the spleen, which is more chronic in its course, there are scattered, yellowish-white, **caseous nodules,** which may reach a third or a quarter of an inch in diameter (*see* fig. 297). This variety is seen specially in children, and, from the resemblance of the pale, caseous nodules in the congested organ to almonds scattered in brown toffee, has been termed "**hard-bake spleen.**" It is sometimes also called "**ape-tuberculosis,**" from the liability of monkeys in captivity to suffer from this form of the disease. The nodules vary somewhat in their consistence, but are often very **soft** and easily washed out, leaving a series of holes on the cut surface. A similar caseous condition is often found in the liver, and, sometimes, in the kidneys, of these cases. **Larger**

tuberculous nodules, *e. g.* up to the size of a walnut or more, may also occasionally be found in the spleens of children, especially if they have suffered from tabes mesenterica.

SYPHILIS does not often produce any very definitely recognisable lesions in the spleen, though, in congenital syphilis and in the rapid febrile forms of the disease, the organ may be **enlarged.** There is usually well-marked, and sometimes extreme, **proliferation of the endothelial cells** lining the pulp-sinuses—a condition which has sometimes been mistaken for an endotheliomatous tumour (*see below*, under **Tumours**). **Gummata** may occur, but are not very common. Deep, irregular **cicatrices,** sending fibrous bands into the interior of the organ, may result from the absorption of these—*cf.* the similar phenomena seen in the liver. Changes in the spleen in syphilis may also be secondary to syphilitic disease of the liver, as well as due to the local action of the virus upon the spleen itself. In the latter case, especially in congenital syphilis in infants and young children, *Spirochæta pallida* may be present in large, and often in enormous, numbers in the spleen-lesions. The relationship of syphilis to **waxy disease** has already been discussed.

LEPROSY.—When this disease has become sufficiently advanced, the endothelial cells of the spleen-pulp are found to be proliferated and enlarged, and may contain great numbers of the causal organism, *B. lepræ.*

HODGKIN'S DISEASE.—This condition, which presents close resemblances to a chronic infective process, usually affects the spleen in a very characteristic manner. For a description of the disease, *see* p. 640.

TUMOURS OF THE SPLEEN.—**Primary tumours** of the spleen are exceptionally rare. **Lymphomas, lympho-sarcomas,** and **endotheliomas** have been described. Certain cases described as endotheliomas, *e. g.* the so-called "primitive endothelioma" of Gaucher, are more probably of the nature of a chronic irritative endothelial proliferation or hyperplasia, than true neoplasms. **Secondary growths** of **cancer** and **sarcoma,** especially **melanotic sarcoma,** *may* occur, but, except where its surface is involved as part of a general peritoneal spread, the spleen, as a rule, escapes the presence of metastases, even when these are numerous in other organs. This may be due to the active phagocytic processes and ferment-reactions which form a large part of the function of the organ.

ANIMAL PARASITES.—**Hydatid Cysts** may occur in the spleen, but are not common. They may be of large size, and are not unusually associated with the presence of similar cysts in the liver. Cysts due to *Cysticerci* and to *Pentastoma denticulatum* have also been found.

Malarial and other protozoal parasites, *e. g.* the **Leishman-Donovan bodies** of Kala-Azar, may pass certain of their developmental stages in the spleen, as well as in the bone-marrow and elsewhere. Reference has already been made to the acute enlargement of the organ during a

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paroxysm of malaria: and to the chronic enlargement which may super-
vene upon a series of such acute attacks. In the latter case, the enlarge-
ment may be very considerable, and the enlarged organ (" **ague cake** ")
is very liable to rupture from injury. There may be thickening of the
capsule from the occurrence of peri-splenitis. The trabeculæ and adenoid
reticulum become coarser; and the condition is usually associated with
chronic venous congestion. The Malpighian bodies tend to become
atrophied; and the most characteristic phenomenon is the marked
proliferation, enlargement and phagocytic activity of the endothelial.
cells, which may contain numerous infected blood-corpuscles and parasites,
and the pigment derived from these.

SPLENIC ANÆMIA or PRIMARY SPLENOMEGALY [1] :—

This extremely chronic disease, which is commoner in males than in
females, is specially characterised by **enlargement of the spleen,** often
enormous in degree, associated, particularly in its later stages, with
extreme **diminution in the numbers of all the formed elements of the blood,**
and, usually, with the occurrence of **hæmatemesis** and **melæna** or, less fre-
quently, of **epistaxis** and other forms of hæmorrhage. The spleen is firm
in consistence, and has a homogeneous pinkish-red colour on section. The
Malpighian bodies are widely separated and usually extremely atrophied,
there being **proliferation and greatly increased phagocytic activity of the
endothelial cells of the pulp,** which ingest red blood-corpuscles and con-
sequently contain a large amount of blood-pigment. There is, in addition,
a progressive **fibrosis** or increase of the fibrous tissue of the organ, due
to thickening of the adenoid reticulum and fibrous trabeculæ. **Hæmo-
rrhages, large infarcts,** and **chronic peri-splenitis,** often with adhesions to
neighbouring structures, are common.

[1] For an interesting discussion on "Splenic Enlargements other than
Leukæmic," by Osler and others, see *British Medical Journal*, October 17, 1908,
p. 1151. Osler, in his introductory paper, gives the following clinical grouping
(which does not profess to be complete) of such splenic enlargements :—
" 1. In children, disturbances of metabolism and in chronic intestinal affec-
tions : Rickets, amyloid disease, and in a large but ill-defined group of intestinal
disorders, particularly in the tropics; the pseudo-leukæmia infantum.
" 2. In the infections : Syphilis, malaria, kala-azar, and other forms of tropical
splenomegaly, Hodgkin's disease and tuberculosis.
" 3. In primary disorders of the blood-forming organs.: Leukæmia, pernicious
anæmia, chlorosis, hæmachromatosis; polycythæmic splenomegaly.
" 4. In cirrhosis of the liver : Syphilitic, alcoholic, hypertrophic of Hanot.
" 5. Hereditary and family forms of splenomegaly : (a) With the congenital
acholuric icterus; (b) with constitutional disturbances, dwarfing, etc.
" 6. New growths and parasites: Sarcoma, primitive endothelioma of Gaucher (?),
Echinococcus, and the *Schistosoma* of Japan.
" 7. Splenomegaly not correlated with any of the above or with any known cause :
Banti's disease, with its three stages of (a) simple enlargement, (b) splenomegaly
with anæmia, (c) splenomegaly with anæmia, jaundice, and ascites."
In many of these conditions, however, the enlargement may be only moderate
in degree, and in some, e. g. pernicious anæmia, it is by no means constant. For
details, reference should be made to the original paper.

In the early stages of the disease, **the blood** may shew little or no alteration. Later, there is diminution of the **erythrocytes** to three, two-and-a-half, or even to two, millions per c.mm. Nucleated and other abnormal varieties of red cell are, however, comparatively uncommon. The **hæmoglobin-percentage** may fall to 30, 25, or even 15. **All varieties of leucocytes** are also extremely diminished in numbers, the total count falling, it may be, to 1200, 1000, 800, or even less—sometimes with slight intermissions.

The **bone-marrow** in two cases which one of the authors had, through the kindness of the late Dr. G. A. Gibson of Edinburgh, the opportunity of examining during life (the specimens being obtained by trephining the tibia), shewed well-marked gelatinous degeneration, with diminution in the number of hæmopoietic cells, which, however, appeared to retain their normal ratio to one another.

The **liver** in this disease may be slightly enlarged, and may shew cirrhotic changes, usually combined with fatty degeneration. When this cirrhotic condition of the liver is well marked, the disease is known as **Splenomegalic Cirrhosis** or **Banti's disease**—jaundice and ascites supervening upon the other symptoms already mentioned. Osler regards these hepatic changes as a late stage of the disease under discussion. Changes in the portal vein, such as endophlebitis, stenosis, and calcification, have been described in a few of the cases, and are probably secondary to the splenic condition.

The main phenomena of the disease appear to be an **abnormally increased capacity of the spleen for blood-destruction,** probably under the stimulation of some toxin: and the **progressive fibrosis of the organ, with secondary changes in the bone-marrow, blood, and liver.** The disease, if not too advanced, has, in many instances, been cured by splenectomy (Osler, Warren, and others, and in several cases investigated by one of the authors).

ANÆMIA or PSEUDOLEUKÆMIA INFANTUM of von Jaksch.—This is a disease of infancy and early childhood, and is commoner in the female than in the male. It is usually chronic in its course, and may be associated with gastro-intestinal disturbance, rickets, or syphilis. It is characterised by **great enlargement of the spleen, and moderate increase in the size of the liver.** There is no leukæmic infiltration of the liver and other organs. The **lymphatic glands** may be slightly enlarged, and the **marrow** is described as shewing an erythroblastic reaction. The **blood** is characterised by marked diminution in the red corpuscles (usually to between three-and-a-half and one-and-a-half millions, or even less in severe cases), nucleated reds being, as a rule, extremely abundant, and shewing degenerative changes, and sometimes mitotic division. Megaloblasts are found in severe and advanced cases. The leucocytes shew a characteristic increase, e.g. from 20,000 to 50,000 or more, in which sometimes the polymorphs, but, more typically, the mononuclears, predominate. Small

numbers of myelocytes have been observed in some cases. Degenerative changes are very common in the white cells.

Ewing[1] is of opinion that some of the cases which have been published may have been of the nature of pernicious anæmia, whilst others may have been leukæmic in nature; but, putting these doubtful cases on one side, others remain which conform to the type described by von Jaksch, in which the blood-picture corresponds with the above description, and the visceral changes characteristic of pernicious anæmia and leukæmia are absent. Ewing suggests that the condition is a return of the embryonic hæmopoietic function of the liver, under the stimulus of some unknown toxic agent.

SPLENECTOMY.—The results of removal of the spleen have been studied **experimentally in animals**; and **in man,** in cases of **injury** and in certain diseased conditions, more especially in **splenic anæmia.** The results in both sets of cases are comparable. The organ is not necessary to life; and its removal is followed by a **transitory fall in the number of red blood-corpuscles,** varying in degree and duration, but usually disappearing in from one to six months or a year. The **amount of hæmoglobin is also diminished,** and **megalocytes** may appear in the circulating blood. There is usually a **distinct increase in the numbers of the leuco- cytes,** somewhat variable in its amount and characters. The polymorphs are, as a rule, the principal cells which shew an increase, but this increase may subside and be followed by a lymphocytosis, and also, it is said, by a characteristic increase in the eosinophils. In some instances, however, all these changes may be comparatively slight, or even absent. Hyper- plasia of the bone-marrow, and also a slight increase in the size of the lymphatic glands, have been described in some cases. Splenectomised animals may exhibit an **increased susceptibility to certain diseases,** for example, the inoculation of the spirillum of relapsing fever into monkeys in which the spleen has been excised, leads to a uniformly fatal result, in place of the regular, periodic attacks and possible recovery resulting in the case of the ordinary animal.

POLYCYTHÆMIC SPLENOMEGALY.—In this condition, the spleen may attain an enormous size. The seat of the primary disease is probably in the bone-marrow, and the phenomena in the spleen are mainly those due to exces- sive hæmolytic activity (i. e. phagocytosis, increase of pigment, etc.). The erythrocytes in the blood of such cases may be more than double their normal number; the hæmoglobin is increased in amount; and the leucocytes may also be considerably increased in number. It has been suggested that some cases of this disease may be analogous to the leucocythæmias—in this instance, the condition affecting the erythroblastic, in place of the leucoblastic, elements of the marrow. (For synonyms and a fuller account of this con- dition, see p. 612.)

[1] Ewing, *Clinical Pathology of the Blood,* 2nd edition, Henry Kimpton, London, 1904, p. 271.

DISEASES OF THE RESPIRATORY· SYSTEM

DISEASES OF THE NASAL CAVITIES

CONGENITAL ABNORMALITIES. — Complete absence of the nose, absence of the septum, and stenosis of the orifices, are very rare defects. Deviation of the septum, and defects due to involvement of the nasal cavities in the conditions of **hare-lip** and **cleft-palate,** are comparatively common (*see* p. 732).

DISTURBANCES OF THE CIRCULATION.—Hæmorrhage from the nose (epistaxis) is common. It may occur without any apparent cause, or it may result from the rupture of over-distended vessels in acute congestion or in chronic venous congestion of the mucous membrane. It frequently occurs in pernicious anæmia, leukæmia, and hæmophilia, and in other conditions in which the blood-vessels are diseased, or the blood-pressure is unduly high, especially in Bright's disease. It is not uncommon at the onset of typhoid fever and other infectious diseases. A certain amount of blood is often mixed with the purulent discharge of **rhinitis,** or with the exudate from inflammatory conditions of the accessory sinuses.

INFLAMMATION :—

(*a*) **ACUTE CATARRH (Acute Rhinitis, Coryza).**—This always results from some specific irritant, and its commonest manifestation is the ordinary " cold in the head," but more intense forms are seen in scarlet fever and in diphtheria. It may be produced by the action of irritant fumes, but is more usually associated with certain infective conditions, such as influenza, measles, typhoid fever, etc. Cold is probably merely a predisposing cause, acting by lowering the vitality of the part. The mucous membrane is at first red and dry, and the vessels are dilated. Very soon, there is exudation of lymph with migration of leucocytes from the distended vessels; and a secretion, at first mucoid, later serous, and then muco-purulent, appears. The organisms associated with this condition are, *Staphylococcus albus* and *aureus*, *Streptococci, Pneumococci,* various *diphtheroids*, *B. pneumoniæ* of Friedländer, *M. catarrhalis,* sometimes *B. influenzæ* and the *Meningococci.* The condition is usually caused by a combination of several of these organisms, and not by any single group.

The **posterior nares** and especially the **naso-pharynx** are important areas for the lodgment of bacteria, and the naso-pharynx is generally recognised as the commonest position in which *Meningococci* are found in carriers, in contact cases and in patients actually suffering from cerebrospinal fever. It has been found that in a considerable number of the carriers of meningococci, **adenoids** are present, and, in others, there are **abnormalities** such as thickening and deformity of the septum, enlargement or deformity of the middle turbinates and narrowness of the nasal cavities, associated with some œdema of the mucosa. All these conditions tend to bring about " contact " of the mucosa, and not only favour the genesis of carriers, but favour also the resistance to treatment.

Cleminson[1] believes that the **accessory sinuses** are the main seat of meningococcal infection in carriers, and that these cavities, being often difficult to disinfect, are able continually to reinfect the upper and more secluded portions of the naso-pharynx.

Adenoids.—Hypertrophy of the lymphatic tissue or **naso-pharyngeal tonsil** in the naso-pharynx, giving rise to " adenoids," is very common in children. These adenoids, as already noted, are an important factor in producing carriers in cases of infection with *Meningococci*, but other bacteria, *e.g.* Pfeiffer's *B. influenzæ*, may also be arrested in these masses of lymphatic tissue, and adenoids may be the starting-point of tuberculosis—the bacilli, air-borne or in milk, becoming lodged in this tissue.

In certain cases, the exudate may be fibrinous, and a whitish false membrane may be produced. This is commonest in inflammation caused by *B. diphtheriæ*. The inflammatory changes may extend so as to involve the various accessory sinuses.

(*b*) **CHRONIC CATARRH.**—This is, very commonly, a sequel of repeated acute attacks, and occurs particularly in syphilitic and in tuberculous subjects. Narrowing of the cavities, especially when due to, or associated with, deviation of the septum, is an important predisposing causal factor. The mucous membrane becomes thickened, especially over the inferior turbinate bones; and, in some cases, polypi may be formed. This **hypertrophic rhinitis** may persist, and frequently it is followed by atrophic changes; dry crusts are formed, and extensive ulceration results. The secretion becomes purulent, and has an extremely offensive odour. To this atrophic condition the term **ozæna** is applied.

GRANULOMATA AND TUMOURS :—

TUBERCULOSIS may present itself in the form of localised tubercle-granulations, or more widely spread ulceration, and is probably most frequently observed on the cartilaginous septum. Lupus may extend from the face so as to involve the anterior nares and nasal cavities.

[1] Cleminson, " Naso-pharyngeal Conditions in Meningococcus Carriers," *Brit. Med. Jour.*, July 20, 1918, p. 51.

SYPHILIS.—Mucous patches occur in the secondary stages of the disease, and the catarrhal condition associated with "*snuffles*" in congenital cases is well recognised. *Spirochœte pallida* may be found in the secretions, but organisms of secondary infection, such as *spirochœtes* of other types and various bacteria, are frequently present.

Syphilitic affection of the nose occurs in the tertiary stage of the disease, gummata being formed either in the mucous membrane or in the deeper tissues. These gummata often involve the bones and cartilages; and ulceration and extensive destruction of the tissues may result. There may be perforation of the septum and of the palate, and destruction of the nasal bones.

TUMOURS.—Mucous and **fibrous polypi,** true **papillomata, sarcomata,** and both **squamous epitheliomata** and **glandular carcinomata** may occur.

The polypi are often the result of inflammatory changes, and may be composed of œdematous granulation-tissue.

FOREIGN BODIES in the nose may become encrusted with lime-salts and form **nasal calculi** or **rhinoliths.**

PARASITES.—Maggots or the larvæ of flies, **sporozoa** (*Rhinosporidium kinealyi*), and **fungi** (*Aspergillus fumigatus*) may occur.

(PHARYNX.—Diseases of the pharynx are dealt with under the **Digestive System.)**

DISEASES OF THE LARYNX

MALFORMATIONS occur, but these are so rare and so unimportant that further reference to them need not be made.

DISTURBANCE OF THE CIRCULATION.—Active hyperæmia, acute and **chronic venous congestion,** and **hæmorrhages** occur, but do not present any special features calling for description.

FOREIGN BODIES, such as particles of food, fish- or meat-bones, coins, buttons, teeth, etc., may gain access to the upper air-passages. If large, they may close the orifice of the glottis, but, more commonly, they give rise to dyspnœa and spasm, with subsequent inflammatory changes.

INFLAMMATION :—

(*a*) **ACUTE CATARRH** of the larynx occurs as a result of chemical or mechanical irritation, or may be caused by some bacterial—or possibly protozoal—or other irritant, as, for example, the catarrh which sometimes occurs during an attack of measles, whooping-cough, smallpox, or typhoid fever. Most commonly, it occurs as an extension or complication of catarrhal inflammation of the throat, trachea, or bronchi. The secretion, which is generally scanty, is at first mucous, and later muco-purulent. The mucous membrane is red and swollen, though the swelling is usually not very great, and does not commonly give rise to any obstruction. The suffocative attacks which sometimes occur in children with acute

laryngitis are due to spasm of the muscles of the glottis, as well as to œdema of the neighbouring soft parts.

(*b*) **CHRONIC CATARRH** may follow the acute form, or it may occur independently of it. Over-use of the voice, or exposure to cold, to irritating vapours, to dust, etc., are among the commoner predisposing causes which damage the tissues and allow bacterial invasion. The mucous membrane is thickened and its surface appears granular, probably the result of enlargement of the racemose glands. Flat, superficial, or crater-like ulcers are found in the region of the posterior commissure, or in the epiglottis and the ary-epiglottic folds. **Microscopically,** the mucous membrane shews an overgrowth of connective tissue. The contraction of this, and the later atrophic changes, may bring about **stenosis of the larynx**—a condition specially seen in syphilitic disease.

(*c*) **ŒDEMA GLOTTIDIS.**—In this condition, there is great swelling of the tissues of the glottis and its neighbourhood, with œdematous infiltration, especially of the looser structures—the whole of the mucous and submucous tissues being involved. As already stated, the œdema may occur during the course of **Bright's disease,** or in so-called **angio-neurotic** cases (which are probably toxic or infective in origin), and also occasionally as the result of idiosyncrasy to certain drugs; but it is associated more commonly with **acute** or **chronic inflammatory affections** of the larynx. Thus, it may occur during an acute catarrhal inflammation, or in connection with diphtheria, the pustular stage of smallpox, and in syphilis or tuberculosis; or it may be brought about by the direct spread of inflammation from adjacent parts, or by the direct action of an irritant, as, for example, the œdema which results from a scald produced by drinking boiling water: or from the action of a strong mineral acid, etc. The parts specially affected are the looser submucous tissues of the ary-epiglottic folds, the ventricular bands, and, to a somewhat less extent, the epiglottis, especially at its base. Sometimes, particularly if the irritant be a septic one, the œdematous infiltration is **semi-purulent** or **purulent ;** and may extend along the submucous tissue of the trachea for some distance below the glottis.

(*d*) **PERICHONDRITIS.**—Inflammation of the perichondrium may be more or less chronic, and give rise to mere induration and swelling; but, more often, pus is formed under the perichondrium. This accumulation of pus cuts off the cartilage from its source of nutrition, and is generally followed by **necrosis.** The **cricoid cartilage** is most frequently affected, but the condition, especially when suppuration has occurred, may extend widely. Commonly a **secondary** result of tuberculosis or of syphilis of the larynx, it may occur as a **primary** condition in cases of typhoid fever, the lesion then being situated towards the base of the arytenoid cartilages and close to the posterior commissure.

(*e*) **MEMBRANOUS LARYNGITIS.**—In this condition, the larynx at first shews hyperæmia and increased mucous secretion. This is succeeded

by the formation of a more or less adherent greyish or yellowish membrane which, on **microscopical examination,** is found to consist largely of fibrin and entangled leucocytes, with also some degenerated and degenerating cells of other varieties. Though, in the majority of cases, this false membrane is **diphtheritic** in origin, and, scattered through it, may be found the Klebs-Lœffler bacillus in association with other organisms, especially *Staphylococci, Streptococci,* and *Pneumococci,* yet, in some cases a membrane, similar in nature, may be produced in other infectious diseases, such as scarlet and typhoid fevers, and also as a result of violent irritation, such as might be caused by the inhalation of steam. A varying degree of necrosis of the mucous membrane—especially in its more superficial layers—is also present.

TUBERCULOSIS OF THE LARYNX is almost invariably **secondary** to tuberculous disease in the lungs, and occurs in two main varieties :—

1. **Minute, shallow ulcers,** which have been preceded by the formation of small tubercle-granulations, may occur in or under the mucous membrane of the vocal cords. These ulcers are found especially on the parts of the larynx where the sputum most readily lodges, *i. e.* near the margins of the cords and on the posterior commissure.

2. There may be **extensive tuberculous infiltration** of the tissues, accompanied by inflammatory œdema and secondary ulceration. In this condition of **laryngeal phthisis,** the tissues of the larynx, especially the ary-epiglottic folds and the epiglottis itself, are swollen, thickened, and ulcerated. The ulcers, at first small, become confluent, show a very irregular outline, and may lead to perichondritis, especially of the **thyroid cartilage,** and to extensive destructive changes. **Microscopically,** the tissues in the deeper parts of the larynx are swollen and infiltrated with inflammatory products, and there are well-marked tubercle-follicles and giant-celled systems. Secondary involvement with other bacteria is frequent, and these bacteria aid both in the production and extension of the ulcerated area.

SYPHILIS OF THE LARYNX occurs in various forms and at any stage of the syphilitic infection. There may be merely a catarrhal condition, or a catarrh with slight erosions of the surface. " **Mucous patches** " or **Condylomata,** which are irregular papillomatous elevations of the mucous membrane, may be present; or there may be irregular infiltration of the structures with granulation-tissue. More characteristic changes, however, are the **deep, irregular ulceration** and extensive infiltration of the whole of the tissues of the larynx. The ulcers cause considerable destruction, not only of the mucous and submucous tissues, but also of the cartilages; and perforation may be brought about. The newly-formed infiltrating tissue undergoes cicatrisation; and irregular contraction and partial stenosis are produced. The syphilitic ulcers are found most commonly at the upper part of the larynx in the region of the vocal cords, but they may occur at other parts, and may bring

about secondary involvement of the trachea and larger bronchi, especially near the main bifurcation. They may give rise to perichondritis, more particularly of the **cricoid cartilage.**

LEPROSY and **GLANDERS** may attack the larynx, producing thickening and ulceration.

TUMOURS are not common, but **papillomata** and **fibromata** may occur. The former grow most frequently from the vocal cords; and the latter, on the cords, or at the base of the epiglottis. Other simple tumours are very rare.

Primary carcinoma may occur, and is of the squamous epithelial type. **Sarcomata** are occasionally found.

PARALYSIS of the muscles of the Larynx may be unilateral or bilateral, and may involve the **abductors** or **adductors** or **both.** The extent will depend on the size and the position of the lesion which involves the nerves of supply. Such lesions may be central, *i. e.* in the brain or spinal cord; or they may be local, as aneurisms, tumours, etc., pressing on the vagus or the recurrent laryngeal nerves: or as neuritis of these nerves themselves, *e. g.* in lead-poisoning, etc. Resulting from this condition, inflammatory affections may be set up in the bronchi and lungs, *e. g.* through the inhalation of food—giving rise to broncho-pneumonia, etc.

DISEASES OF THE TRACHEA

CIRCULATORY DISTURBANCES, similar to those seen in the larynx, to which reference has already been made, may also occur in the trachea.

COMPRESSION by aneurisms, mediastinal growths, etc., may take place; and, as a result of the erosion by an aneurism, or the necrosis and suppuration produced by breaking down glands, perforation may occur.

INFLAMMATORY CONDITIONS are generally the result of the extension of a laryngitis or a bronchitis, and present much the same features as are observed in the larynx or in the bronchi.

GLANDERS : WOOL-SORTERS' DISEASE.—The local lesion consists of swollen patches, often with considerable hæmorrhage into them, in the mucous membrane in the lower part of the trachea and the large bronchi. The tissues are inflamed and œdematous, and ulceration may be present. There is always associated enlargement of the mediastinal and bronchial glands, and hæmorrhagic infiltration of the cellular tissues of the region. There are pericardial and pleural effusions, hæmorrhages into the serous membranes, and congestion, collapse, and œdema of the lungs. In the local lesions, *B. mallei* is present, usually in large numbers.

TUBERCULOSIS and **SYPHILIS** also occur under the same conditions, and produce much the same lesions, as in the larynx. Further reference, therefore, need not be made to them.

TUMOURS.—**Primary tumours** are rare. **Secondary cancers** or **sarcomas** which have spread from the œsophagus, thyroid gland, or surrounding lymphatic structures, may occur.

DISEASES OF THE BRONCHI

In studying the diseases of the bronchi, it is essential to recall some of the more important points in the histological structure of these tubes. The mucous membrane is covered by a layer of columnar ciliated epithelium, beneath which there is a translucent homogeneous basement-membrane. Between the basement-membrane and the muscular coat, there is a layer of vascular connective tissue containing elastic fibres, in which masses of lymphoid tissue occur. The muscular coat or bronchial muscle (muscularis mucosæ), which is really the deeper part of the mucosa, consists mainly of

Fig. 298.—Transverse Section of a Normal Bronchus, shewing the various structures mentioned in the text.   × 30.

circular fibres, with, however, a few longitudinal ones. External to the muscularis mucosæ is the adventitial coat, composed of loosely arranged connective tissue, which is continuous with the interstitial connective tissue of the lung. In this adventitial coat, the mucous glands and the cartilages are situated. In the **smaller divisions** of the **intra-pulmonary bronchi,** the adenoid tissue becomes gradually reduced in amount until, in the very minute branches, no trace of it can be found. In like manner, the cartilages become irregular and smaller, and finally disappear. On the other hand, the muscularis mucosæ becomes thicker. The epithelium also alters in character, becoming more cubical, or even flattened in the terminal branches. On this difference in histological structure depends,

to a certain extent, the variations in the character of the lesions which
are found in different parts of the bronchial tree, even although these
may in each case be produced by the same irritant. Thus, diseases of the
larger bronchi resemble those of the **trachea,** with which their structure
closely corresponds, and do not tend to spread to the adjacent lung-tissue;
whereas affections of the **minute bronchi** are more closely allied to those of
the **lung-parenchyma,** and tend to spread to it.

INFLAMMATION.—Inflammatory changes in the bronchi vary much
in intensity. In the slighter forms, the larger and medium-sized tubes

Fig. 299.—Metal Cast of a Small Bronchus and Bronchioles, shewing the Bulbous Terminal
Vesicles or Infundibula. (Made by C. W. Cathcart, C.B.E., F.R.C.S.E.) × 6.

are mainly affected. Where the minuter divisions of the bronchial tree
are inflamed, the condition is generally, if not always, associated with
accompanying disease of the lung-parenchyma. Thus, in describing
Bronchial Catarrh or **Bronchitis,** it will be convenient to limit the descrip-
tion to inflammatory changes in the larger and medium-sized bronchi,
leaving the changes in the smaller branches to be dealt with under
Broncho-Pneumonia.

(1) **ACUTE BRONCHITIS OR BRONCHIAL CATARRH.**—This con-
dition, when not associated with inflammation of the lung-parenchyma,
is mainly confined to the medium-sized intra-pulmonary bronchi; and
may arise from exposure to cold, the inhalation of irritant vapours, or
by extension from a laryngitis or a tracheitis. The condition is very
commonly associated with infectious fevers. The organisms most

frequently present are *Pneumococci* and *Streptococci*, but *B. influenzæ*, *M. catarrhalis*, *B. pneumoniæ* of Friedländer, and other bacteria may be found. The mucous membrane appears swollen, and is of an intensely red colour. In the **early stage,** the membrane may be dry, but, **later,** it becomes covered by a mucous, muco-purulent, or a purulent secretion. The **secretion,** at first viscid, tough, and more or less translucent, is largely composed of mucin, which is poured out in excessive amount from the inflamed mucous glands. In the later stages,

Fig. 300.—Transverse Section of a Bronchus in a case of Acute Bronchitis. Note the very marked infiltration of the mucosa with inflammatory cells, the separation and swelling of the muscularis mucosæ, the swelling of the basement-membrane, and the irregular appearance of the lining cells.   × 45.

it becomes less tough, more opaque, and yellowish-white or greenish in colour, owing to the infiltration of the mucin with the cellular and fluid products of the inflammatory process. Usually, the cellular content, in the early stages, is not high and consists mainly of a few leucocytes, red blood-corpuscles and a few cylindrical epithelial cells (bronchial cells). There may be some mononucleated cells—the so-called "mucous corpuscles," derived probably from lymphatic masses along the tract. Later, when the muco-purulent stage is reached, the inflammatory cells (pus-cells) are very greatly increased and the epithelial cells have lost their shape and show various degenerations. **Microscopically,** there is general congestion with swelling of the mucous membrane, due to the dilatation

of the vessels and the transudation of lymph from them (*see* fig. 301). The lining epithelium is swollen, and the cells undergo proliferation and separation—sometimes in irregular masses—from the basement-membrane, which itself undergoes irregular swelling. The mucosa becomes infiltrated with leucocytes, and its fibres and the fibres of the muscularis mucosæ are separated from one another and swollen by the accumulation and imbibition of the transuded lymph. The mucous glands shew marked catarrhal changes.

Fig. 301.—*Lung*—Acute Bronchitis—shewing congested vessels, thickened basement-membrane, proliferation of lining epithelium, and exude in the lumen. (The blank area in the centre is an artefact due to retraction of the exudate during embedding.) × 300.

(2) **CHRONIC BRONCHITIS** occurs after repeated attacks of the acute form, especially in people who have some intercurrent affection of the heart or lungs which keeps up a congestion of the mucous membrane. The secretion is often very abundant, and frequently presents all the characters of pus. It may be pigmented from the presence of carbon-pigment or of altered blood. The mucous membrane is congested, and often shews a brownish-red, or even a slaty-blue, pigmentation. Sometimes, especially in the so-called **sub-acute** cases, the **sputum** is tenacious, viscid and very small in amount. Where the bronchitis is associated with emphysema, the quantity of sputum may vary considerably, and

may consist of gelatinous or frothy mucus, or yellowish-white muco-purulent exudate, often tinged with blood. It usually contains greater or smaller numbers of pus-cells and may shew blood-cells and pigmented alveolar epithelium. Occasionally, eosinophil cells are found, but these are more characteristic of true cases of **Asthma.** The lumen of the bronchus may be dilated, and its normal corrugated appearance be to a large extent lost. **Later** in the disease, the mucous membrane becomes thinned and atrophied, and through it the fibrous and cartilaginous framework of the bronchus becomes more apparent. **Minute ulcers,** just visible to the naked eye, are sometimes seen between the cartilage-rings. On **microscopical examination,** the epithelial changes are very pronounced, almost the whole of the ciliated cells having disappeared. They may, in parts, be replaced by columnar or polygonal epithelium, the mucous membrane becoming thinned and atrophied. The basement-membrane shews irregular thickening. The mucosa and sub-mucosa may shew very considerable swelling, the vessels be much dilated, and the mucous glands shew a condition of **chronic catarrh** and **atrophy,** some of them, it may be, becoming **cystic** from obstruction to their ducts. The mucosa is infiltrated with cells, mostly of the mononucleated type, and presents the appearance of vascular granulation-tissue. At a later stage, the loose vascular structure of the mucosa may be replaced by well-formed fibrous tissue, which spreads to the lung-parenchyma. The cartilages may undergo degenerative changes and partial absorption, whilst the muscular tissue becomes infiltrated with inflammatory cells, and may atrophy and be replaced by fibrous tissue.

The bacteria associated with this condition are the same as those found in acute cases, viz. *Streptococci, Pneumococci, B. influenzæ,* or, at any rate, Gram-negative bacilli practically indistinguishable from this organism, *M. catarrhalis, B. pneumoniæ* of Friedländer, etc.

(3) **MEMBRANOUS OR PLASTIC BRONCHITIS.**—This condition is characterised by **spasmodic** attacks, which come on suddenly, and, during which, **casts** of portions of the bronchial tree are expectorated. The attacks are often preceded by hæmorrhage. These casts are whitish or greyish-white in colour, and branches, corresponding to the divisions of the bronchi, are seen if the cast is floated out in water. The mode of their formation is unknown. They are generally regarded as being composed of masses of fibrin, and hence the condition has been called " **Fibrinous Bronchitis."** In some cases, however, the cast is composed mainly of masses of epithelial cells, with little or no fibrin. Similar casts, which are definitely **fibrinous** in character, are sometimes seen in the bronchial tubes in cases of diphtheria; and, in cases of acute pneumonia, a fibrinous exudate may form in the smaller bronchi, giving rise to casts, which may be expectorated.

STENOSIS, SPASMODIC CONTRACTION, AND DILATATION :—

STENOSIS OF THE BRONCHI may be caused from without by the pressure of tumours or aneurisms. Tumours, especially sarcomata of the mediastinum, may extend along the bronchi, compress and invade their walls, and thus cause very considerable narrowing or even complete obstruction.

Narrowing also results from **spasmodic contraction** of the muscular wall; and it is generally held that, in **asthma,** this narrowing of the finer bronchi is the essential pathological change, the muscular spasm being the result of nervous agencies. It is doubtful whether the muscular spasm is the sole cause of the asthmatic attacks, for there is always, associated with these attacks, actual swelling of the mucous membrane, and generally also the presence of exudate, which may be of a fibrinous nature. The small octahedral Charcot-Leyden crystals, which Leyden considered as causal of the muscular spasm, cannot now be thus regarded.

DILATATION OF THE BRONCHI (BRONCHIECTASIS).—Probably, in most cases, this condition is produced by several causes which operate together. Of these, two of the most important are increased intra-pulmonary pressure, and weakening of the walls of the bronchi. The increased intra-pulmonary pressure is commonly associated with bronch-itis or laryngeal stenosis; whilst the weakening of the walls of the bronchi may be congenital, or may result from prolonged inflammatory changes and retention of secretion, which occurs round a foreign body such as a tooth, a collar-stud, fragments of food and the like, which have been inhaled into the bronchus and become impacted. The smaller bronchi are much more liable to become bronchiectatic than the large ones, and, in such conditions as broncho-pneumonia, dilatation of the bronchioles is frequently observed. This is common in acute broncho-pneumonia in children, but it is specially marked in those cases in which resolution is delayed and incomplete and in which a fibrosis of the affected lung-tissue has occurred, and is usually most marked in the lower parts of the lower lobes. In cases of **congenital atelectasis,** in which portions of the lung do not expand at birth, and remain unexpanded, the bronchial walls are usually not so well developed as in other parts of the lung. The dilating force, in these cases, must be the action of the inspired air. Old-standing inflammatory changes act, not only by weakening the walls of the bronchi, but by producing an overgrowth of fibrous tissue in the surrounding lung. This fibrous tissue, by its contraction, pulls on and dilates the walls of the bronchi, especially if the pleural sac is obliterated by adhesions. The dilatation which occurs in the various forms of interstitial pneumonia is due largely to this dragging on the tubes by the newly formed and contracting fibrous tissue. In chronic phthisis, too, the bronchiectasis is in part due to the same cause, though the weakening of the walls by tuberculous ulceration and inflammatory changes set up

by the decomposition of the retained secretions, and by the loss of support due to the destructive processes in the lung, must play an important part. The direct cause of the dilatation, in the majority of cases, is the increase in the intra-pulmonary pressure produced by coughing.

Morbid Anatomy.—The dilated bronchi may be **sacculated** or **digitate.** The sacculated form is seen especially in the various forms of tuberculosis, where local inflammatory and destructive processes are at work. The dilated tubes may assume the form of large, irregular cavities. These have usually a definite lining membrane, and direct communication with an open bronchus can generally be made out.

In the digitate or cylindrical form, the medium-sized bronchi, throughout a considerable part of the lung, are unduly widened, the cause here being a more or less general one, such as prolonged bronchitis. The dilatation may be regular, but, more commonly, the tubes shew a diffuse, irregular beading. This digitate or cylindrical form is seen in the smaller bronchi in cases of pneumonia.

Morbid Histology.—The microscopical appearances of the dilated bronchi vary considerably, the variation depending, to a certain extent, on the exciting cause. If the inflammatory changes are marked, the tissues of the wall are infiltrated with inflammatory cells, and the normal structures are more or less altered or destroyed; whilst, in other cases, the structures of the wall may be thinned and stretched, but can all be distinguished. The epithelium lining the cavity may be intact, or it may be destroyed, and the whole mucous membrane may be replaced by granulation-tissue. The **secretion,** or **exudate** —generally abundant—has a very foetid odour. It is usually greyish or greyish-brown in colour, fluid, and purulent; though, in some cases, it is thick, viscid, and blood-stained. Pus-cells are found in considerable numbers; **elastic tissue** may be present when destruction of the walls is taking place; fatty-acid crystals, cholesterol-, and hæmatoidin- crystals are sometimes found; and alveolar epithelial cells containing pigment, mucin, or fat, are generally present. Occasionally, calcium salts are deposited, giving rise to the so-called **lung-stones.** In addition to various pathogenetic bacteria, putrefactive organisms are present in considerable numbers.

ASTHMA.—Though there are no characteristic pathological changes in asthma, the **sputum** is very typical. During the attack, it may be scanty, containing thick glairy mucous balls in a clear, frothy mucus. These mucous balls are translucent to pale-grey or greyish-yellow in colour, and contain mucous moulds of the smaller tubes, which are cylindrical or sausage-shaped masses of thick mucous threads or spirals or definite **Curschmann's spirals.** In the sputum are found alveolar cells and **eosinophil** leucocytes. The Curschmann's spirals occur in practically every true case of bronchial asthma, and are found particularly at the end of the paroxysm. They consist of a mucous mantle, containing eosinophil and epithelial cells and a refractile central

fibre of altered mucus which is often subdivided into fine fibrils. They are found also in some cases of chronic bronchitis without symptoms of asthma. Various organisms, *e.g.* capsulated streptococci, are of frequent occurrence in the bronchitic casts in asthma, though their causal relationship to the disease is not established.

TUMOURS :—

Primary cancers arising from the mucous glands have been described, but are very rare. **Fibromata, chondromata,** and **lipomata** may occur; and **secondary growths,** both **cancerous** and **sarcomatous,** may involve the bronchi.

DISEASES OF THE LUNGS

- **GENERAL FACTS.**-- Brief reference must be made to certain anatomical considerations which have an important bearing on the distribution and the character of pathological conditions in the lung.

Fig. 302.—" Fusible metal " Cast of a Bronchiole and its Infundibular Passages, etc., shewing the saccular appearance of the Infundibula. (Made by Chas. W. Carthcart, C.B.E., F.R.C.S.E.) ×7.

In the walls of the lung-alveoli there is a considerable amount of elastic tissue, in which is embedded a rich network of capillaries which are the terminal branches of the pulmonary artery. The alveoli are lined by flattened cells of an endothelial type, and communicate with the terminal branches of the bronchioles. Besides the pulmonary arterial supply, there is, in addition, a supply from the bronchial arteries. The latter nourishes the walls of the bronchi and the connective-tissue framework of the lung itself. The return circulation for both the pulmonary and the bronchial arterial supply is mainly carried on through the pulmonary veins. The distribution of the lymphatics of the lungs is of very considerable importance, for it is mainly along these

passages that irritant materials are carried to different parts of the organ. They are found in the walls of the alveoli, and also pass along the walls of the bronchi and the vessels. Another system of lymphatics commences immediately beneath the pleura, and penetrates along the various septa of the lung. The lymphatic trunks leave the lung at its root. Particles inhaled into the small bronchi and alveoli readily pass into the lymphatic system, and are carried along the lymphatic channels by phagocytic cells and lodged in the fibrous-tissue framework of the lung itself, e. g. in the subserous connective tissue, inter-lobular septa, peribronchial tissue, etc., and in the lymphatic glands and elsewhere.

MALFORMATIONS :—

Complete congenital absence or extreme smallness of one or both lungs has been described. Absence of one or more lobes has also been noted by some observers. Other abnormalities, e. g. in the number and size of the lobes, and the presence of additional sulci, are common. Congenital abnormalities of the pulmonary vessels occasionally occur, such as absence of one of the pulmonary arteries —a bronchial, or even an inter-costal, artery coming directly from the aorta, enlarging and taking its place.

INJURIES.—There seems little doubt that clean perforating bullet-wounds of the chest may produce no serious pathological change, and that the patients may recover quickly and completely. But, in the majority of cases, there is added to the simple puncture the effects of laceration, contusion and hæmorrhage and bacterial infection. The actual amount of destruction will, of course, depend on the shape, size, direction, and velocity of the penetrating missile. The lung-wound, in the majority of fatal cases, is characterised by laceration and bruising, with wide extravasation of blood into the tissues surrounding the track. **Pneumothorax** is not common in these cases, but **hæmothorax** occurs in a considerable proportion. If the lung is healthy, hæmothorax generally causes collapse and hinders the spread of infection. Localised sepsis is common in these cases and may occur in both collapsed and uncollapsed lungs; but the spread of the inflammatory area, producing patches of **septic broncho-pneumonia** at some distance from the original wound, is, according to Henry and Elliott,[1] unusual in the collapsed lung. According to these authors, the septic broncho-pneumonia starting from the wound and spreading throughout the lung is always most marked in cases of lung-laceration without hæmothorax, but, when hæmothorax occurs, the laceration is relatively harmless.

GAS-POISONING.—The effects of such heavy gases as **chlorine** or **bromine** have been specially investigated, and chlorine was largely used as the drift-gas for offensive purposes during the late war. The immediate effect was to produce **asphyxia** and death. If, however, the subject survived immediate asphyxia, great dyspnœa supervened. Intense **congestion** of the mucosa of the trachea and larger bronchi was produced; the

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[1] Henry and Elliott, "Morbid Anatomy of Wounds of the Thorax," *Jour. R.A.M.C.*, vol. xxvii., p. 525.

tubes became filled with a thin, light-yellow, frothy secretion, which was richly albuminous. The lungs shewed intense œdema and congestion, with irregular areas of emphysema—apparently produced acutely. Various stages of this œdema and congestion were found in different cases. Such cases often had a very slow and prolonged convalescence, and were liable to chronic bronchitis and various secondary infections.

With **phosgene-gas** the results, in the lungs and air-passages, were very similar to those obtained with chlorine, though capillary thrombosis in the lungs was frequently found. The pathology of the effects of **mustard-gas** was different. After a latent period of twenty-four hours, an intense inflammatory action set in which brought about complete necrosis of the bronchial mucous membrane. At a later period, in those who recovered, fibrosis occurred around the lumen of the bronchi, and a great tendency to bronchitic attacks was a sequel.

DISTURBANCES OF THE CIRCULATION :—

(*a*) **ACTIVE HYPERÆMIA.**—This is, usually, the result of some infective process, or is produced by the inhalation of irritating fumes or gases, or of organic or inorganic particles which act as mechanical irritants. It is a marked feature of the inhalation of " poison-gas," is often present after ether-anæsthesia, and is almost a constant feature in all acute infective diseases, whether of bacterial or toxic origin, *e. g.* measles, septicæmia, etc. It is very often only an early stage of acute inflammation of the lung, the vessels in the alveolar wall shewing marked dilatation, and the alveolar spaces containing lymph or even blood. A **collateral hyperæmia** sometimes develops in one part of a lung, when there has suddenly arisen a considerable degree of obstruction to the pulmonary circulation in another portion of the organ. Thus, embolism or thrombosis of the pulmonary artery may produce collateral hyperæmia.

(*b*) **PASSIVE HYPERÆMIA OR VENOUS ENGORGEMENT.**—Venous engorgement may occur **rapidly,** especially in conditions which lead to embarrassment of the heart's action, such as results from weakness, from cerebral conditions, *e.g.* epilepsy, coma, etc., and also in cases where thrombosis of the pulmonary veins has occurred; but it is generally a **slowly** developed and chronic condition, and is commonly described under the term **Chronic Venous Congestion.** It is due to anything which prevents the free outflow of blood from the lungs, the commonest cause being disease of the heart, due either to some valvular lesion which interferes mechanically with the pulmonary circulation, or to muscular weakness of the heart lessening its driving power. The cardiac valvular lesion which gives rise to this condition in its most pronounced degree is stenosis or incompetence of the mitral valve. Even when, by hypertrophy of the various chambers of the heart, and especially of the right ventricle, circulatory compensation seems to be established, there is still an increase of pressure in the pulmonary circulation, and, in consequence,

a condition of venous engorgement. If compensation is not established, the engorgement becomes much more pronounced; and indurated, ill-defined patches, varying considerably in size, and often situated towards the lower part of the lung, are produced. They are specially abundant where there has been a large amount of capillary hæmorrhage. The lung, especially at these areas, is of a dark brick-red colour, and tough and indurated in its consistence. This condition is very commonly described as **Brown Induration,** but Hasse originally used this term for irregular patches of lung-tissue in which the air-spaces became filled with pigmented
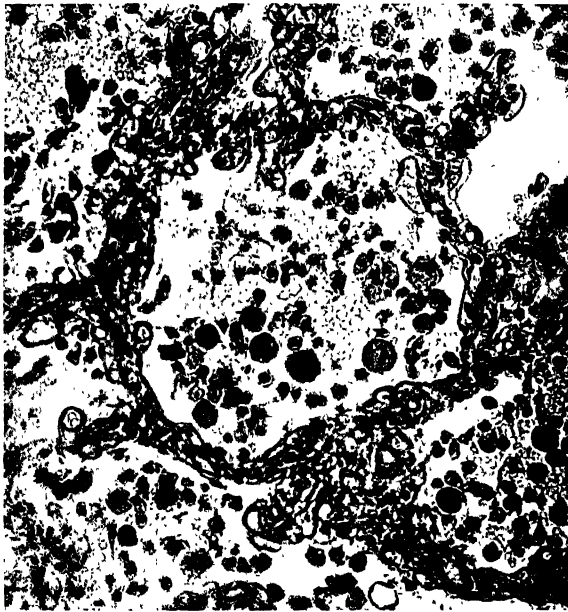
Fig. 303.—Lung in Chronic Venous Congestion, shewing varicosity and thickening of the alveolar capillaries, and the presence of catarrhal cells and blood-corpuscles in the alveolar spaces.   ×. 200.

cells, and which were probably areas of old infarction. There was not necessarily chronic venous congestion associated with them. **On micro-scopical examination** of typical cases of chronic venous congestion, the veins and capillaries are distended, those in the alveolar septa being very prominent, giving to the latter a beaded appearance. The walls of the distended vessels are much thickened. The alveolar spaces contain blood and catarrhal cells in varying quantities, and, in some areas, the lung is rendered almost airless by this filling up of the air-spaces. The catarrhal cells originate mainly as proliferated and cast-off cells from the endothelial lining of the alveoli. They are phagocytic, take up red blood-corpuscles and pigment derived from these, and also any particles of carbon which may be present, pass into the lymphatics of the alveolar walls, and are carried to the peribronchial and perivascular

lymphatics, to the lymphatics in the deep layer of the pleura, and to the bronchial glands—in all of which situations they deposit their pigment. In addition to the thickening of the walls of the veins and capillaries, there is also an increase of fibrous tissue throughout the lung. In this thickened fibrous tissue, and also in the alveoli, the pigment, derived from the blood, is present in the form of brown granules. It is probable that this pigment, by the irritation of its presence, is responsible for, at any rate, part of the fibrous overgrowth which is so constantly found in the lung in this condition.

Fig. 304—Large Pulmonary Infarct, shewing the wedge-shaped, hæmorrhagic area towards the lower margin of the lung, and thrombosis of the corresponding branch of the pulmonary artery.

The vessels in the bronchial wall, and especially those of the smaller bronchi, where there is an anastomosis between the pulmonary and bronchial circulation, become distended. In addition, there is a thickening of both the mucous and submucous coats of the bronchi, leading to catarrhal changes and even to obstruction. Hæmorrhage may occur from rupture of the over-distended vessels in the bronchial walls or in the lung-alveoli.

The sputum, especially in cases due to disease of the mitral valve, consists of white mucus with areas of " rusty " colour, or of a uniformly rusty mucus. The colour is due in part to blood, but mainly to alveolar epithelial cells loaded with golden-yellow amorphous pigment derived from the red blood-corpuscles.

(c) **PULMONARY INFARCTION** frequently occurs in the lung in cases of chronic venous congestion. The raised, dark plum-coloured areas stand out prominently on the surface of the lung. This subject is fully dealt with under **Circulatory Disturbances** (see p. 158), and need not be further referred to here, except to say that the **sputum,** in these cases, consists of tenacious mucus mixed with pure blood or balls of glairy mucus streaked with blood. Microscopically, the red blood-corpuscles are very abundant, and there are few leucocytes or other cells. This characteristic of the sputum is lost in a few days.

(d) **PULMONARY EMBOLISM AND THROMBOSIS.**—Pulmonary emboli arise usually from vegetations on the right side of the heart,

thrombi in the right auricle or ventricle, or thrombi in the systemic veins. These emboli do not necessarily produce infarction. If they are septic, softening of the wall of the vessel may take place and definite aneurisms be formed. This condition of **embolic aneurism** in the lung is rare— only five or six cases being described in this country, and three of these resulted from the detachment of vegetations in the valves and one from a thrombus in the veins of the leg.

Emboli giving rise to pyæmic abscesses are dealt with on pp. 148 and 696. The subject of embolism and thrombosis in the lung is discussed in Chapter V., p. 158.

ŒDEMA OF THE LUNGS is very common where there is general weakness of the heart, or where the circulation is in any way embarrassed. Thus, it is practically always present in debilitating diseases, especially if the patient is confined to bed, in most forms of anæmia, and in cardiac disease where, from any cause, there is venous engorgement. In cases of chronic Bright's disease, it occasionally develops very rapidly from some unknown cause, and, in these cases, the change may be confined to one lung, or even to a part of one lung, e. g. the upper lobe. This is said also to occur in cases of arterio-sclerosis without, at any rate marked, changes in the kidney.

Though sometimes, as in Bright's disease, occurring without hyper-æmia, the condition is almost constantly associated with acute or chronic venous engorgement. The posterior and basal parts of the lungs are usually most affected, gravitation being probably an important deter-mining factor. Thus, if the patient is going about, the lower lobes are specially involved; whereas, if he is lying in bed, it is in the posterior parts that the most intense degree of œdema is found. This œdema is partly inflammatory in nature and due to lymph exuded from the distended vessels. In cases in which the congestion is a marked feature, and where the œdema is specially present at the lower part of the lobe, the term **Hypostatic Engorgement** or **Hypostatic Congestion** has been applied to the condition. The affected parts present, after death, a dark blue or purplish-red colour, and the tissue is more solid than normal. If the lung is incised and squeezed, a frothy fluid, usually mixed with blood or blood-pigment, is expressed from the cut surface. **On microscopical examination,** the capillaries are seen to be distended, and the alveoli contain some granular material—indicating the presence of serous fluid— and perhaps a few blood-corpuscles. Catarrhal cells, in larger or smaller numbers, may also be present.

The sputum may be frothy, colourless or blood-stained, and very watery.

In œdema without venous congestion, the lungs are usually pale, and a clear, pale yellow, frothy fluid can be expressed in considerable quantities from the cut surface. This condition is often well seen in cases of pernicious anæmia.

COLLAPSE AND ATELECTASIS :—

The term **Atelectasis** has been applied to two distinct conditions—one in which the lung has never been properly expanded with air, and the other in which the previously expanded lung has become compressed or collapsed. The latter should be called **collapse.**

CONGENITAL ATELECTASIS—or **ATELECTASIS PROPER**—is found in new-born infants where the inspiratory power has been insufficient to expand the lungs, and is, of course, complete where death of the fœtus has occurred *in utero.* Deficiency of inspiratory force may result from general weakness, from compression of the thorax, or from interference with the respiratory centres by cerebral hæmorrhage; or it may be produced by obstruction of the air-passages by foreign material, *e. g.* meconium or mucus.

The commonest situation in which the condition is found is in the lower lobe, especially its posterior part, though in many cases it may be more widely spread, and may be seen in the middle lobe of the right lung, the edge of the left lung where it overlaps the heart, or even involving the whole of one lobe. The unexpanded area is usually dark-reddish in colour, very tough in consistence, quite airless, and depressed below the level of the surrounding lung-tissue. In its general **naked-eye** appearance, the condition cannot be distinguished from **true collapse,** but, on **microscopical examination,** the collapsed lung usually shews, in its alveoli, catarrhal cells and inflammatory exudate, and frequently, also, inflammatory changes are present in the bronchi; whereas, in the unexpanded lung, if the child is stillborn or dies soon after birth, these appearances are absent, and the part can be inflated from the communicating bronchi. If the patient lives, proliferative changes take place in the connective tissue, the walls of adjacent septa may become adherent to one another, and thus an actual obliteration of the lung alveoli may occur. Some of the cicatrix-like marks sometimes seen in the adult lung are supposed to result from the atrophy of these unexpanded areas.

Secondary dilatation of the bronchi and bronchioles may occur in consequence of atelectasis, and, by some authors, is regarded as compensatory.

COLLAPSE.—Collapse of the lung after it has become expanded may occur in young infants, and cannot, without microscopical examination, be distinguished from congenital atelectasis; but the variety of collapse to which reference is now specially made is that which occurs later in life. It may involve practically the **whole** of the lung, or it may be **partial** in its distribution.

(*a*) **Collapse of the entire lung** may result from compression of the organ from without by pleural effusions or by large tumours. The lung is compressed backwards and inwards towards its root. It becomes of a slaty-grey colour, and is very tough and fleshy in consistence. If the condition persists for a long period, atrophy of. the aërating tissue

of the lung takes place, accompanied by dilatation of some of the bronchi, especially the larger ones, and by a fibrous overgrowth of the connective tissue in the deep layer of the pleura, the inter-lobular septa, and the peri-vascular and peri-bronchial sheaths. The blood-vessels become thrombosed and partly obliterated by endarteritis. The portion of lung immediately adjacent to the root often escapes, even in very extensive collapse.

(b) **Collapse of portions of the lungs** is very common, and may be the result of any condition which tends to reduce the internal, or increase the external, pressure on the tissue of the lung. Thus, all conditions which diminish the inspiratory force or obstruct the entrance of air into the lungs, tend to produce collapse; and these factors are often aided by conditions which mechanically compress the lung and force out the air.

W. Pasteur [1] and others have described a lobar collapse due either to a complete paralysis of the inspiratory muscles—the intercostals or the diaphragm—or to a reflex inhibition of the respiratory movement of the diaphragm. This latter condition is sometimes seen after abdominal operations, but, in these cases, there is, very commonly, a muco-purulent secretion in the bronchi, and this obstruction may, of itself, or aided by the loss of muscular movement, bring about the collapse. It seems to us somewhat doubtful whether the reflex inhibition of the diaphragm, which Pasteur suggests is due to irritation of the afferent nerves of the peritoneum during the operation, plays a very important part in this condition. Inflammatory lesions in the abdomen or pleurisy would impair the movements of the diaphragm, and no doubt this impairment would aid the accumulation of muco-purulent secretion and favour collapse.

Our opinion is that these cases of post-operative collapse of the lower lobe of the lung are, in the majority of cases, due to a purulent bronchitis aided by a relative immobility of the diaphragm, and that this immobility is not usually brought about by any nerve-irritation at the operation, and may, in fact, occur in abdominal conditions, such as distension from enlarged spleen or liver, gaseous distension of the intestines, etc.

Weakening of the thoracic wall, e. g. in rickets, deformities of the chest such as scoliosis, weakening of the thoracic muscles in certain forms of paralysis, or even in cases of general debility, act by diminishing the inspiratory force; whilst distension of the abdominal cavity with fluid, tumours, etc., enlargement of the heart or effusions into the peri-cardial sac, tumours in the thorax, or even the recumbent position of a weakened patient, will act by impeding the full expansion of the lungs.

Obstruction to the entrance of air into the lungs may be produced by pressure on the bronchi by aneurisms or tumours, causing a diminution, or even an obliteration, of the lumen. This diminution or obliteration

[1] W. Pasteur, *The Lancet*, November 7, 1908, p. 1351.

may also arise from the presence of a membranous exudate in the larger
bronchi, as in diphtheria, or the presence of foreign bodies, blood, or
bronchial secretion in the smaller divisions of the bronchial tree.   Direct
pressure forcing out the air is a very important factor.   Thus, in pleurisy
with effusion, empyema, hydro-, pyo-, hæmo-, or pneumo-thorax, collapse
of portions, and perhaps the greater part, of the lung is a usual sequel.

The commonest sites of partial collapse are the lower and posterior
parts of the lungs, the free edges at the base. the middle lobe of the right
lung, and the edge of the left lung where it overlaps the heart.
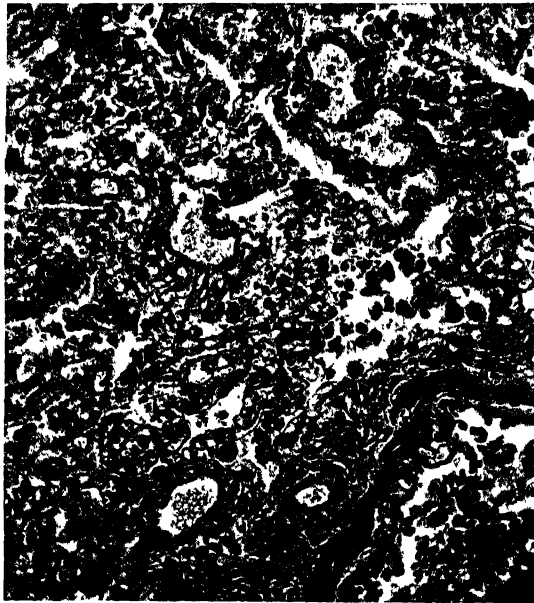
Fig. 305.—*Collapse of Lung.*   Note the folding and compression of the air-spaces, and the
beaded appearance of the capillaries in their walls.   A section of a bronchus, blocked
by inflammatory exudate, is seen at the lower right-hand corner of the figure.   × 200.

Morbid Anatomy.—The collapsed areas are usually irregular in shape,
but well defined in outline.   They are of a dark slaty-blue or purple colour,
are **depressed below the general surface,** and their margins correspond
to interlobar septa.   If the condition is uncomplicated, the pleura over the
collapsed patches is glistening, and shews no evidence of acute inflamma-
tion.   On section, the lung is smooth and firm, dark brownish-red in
colour, and often almost airless and bloodless.   It may sink in water.
Because of the collapse of the intervening air-tissue, the bronchi and
blood-vessels are huddled together, and thus *appear* more numerous than
normal.   **On microscopical examination,** the walls of the air-spaces are
folded and compressed, and may be in contact with one another, their
cavities being completely, or almost completely, obliterated.   Chronic

venous congestion and catarrhal changes are practically always found associated with the collapse, and some of the air-spaces, lined by polyhedral or rounded cells similar to those seen in the fœtus, may be seen in a partially collapsed state.

Lobular Collapse is commonly associated with capillary bronchitis, especially in children, and is rapidly followed by acute congestion, and, later, by lobular pneumonia. Very frequently, around these areas of lobular collapse there is a zone of lobular emphysema. On naked-eye examination, a roughly polyhedral outline, corresponding to the collapsed lobules or groups of lobules, is observed.

EMPHYSEMA :—

Two varieties of pulmonary emphysema are described, one in which the air is contained within the abnormally dilated air-vesicles (**Vesicular Emphysema),** the other in which the interstitial tissue of the lung is its site (**Interstitial Emphysema).**

VESICULAR EMPHYSEMA is very common and may be seen in two forms, the " **small-lunged** " or **atrophous,** and the " **large-lunged** " or so-called " **hypertrophous."**

(*a*) In **Atrophous Emphysema,** the lungs are small in size and may not overlap the pericardium. They are pale in colour, and may weigh only eight or nine ounces. **On section,** the lung-tissue is pale and dry, and hardly any fluid can be expressed from it. **On microscopical examination,** the vesicles are distended, but the main feature is a thinning and atrophy of the inter-alveolar septa. The condition is specially associated with, and caused by, the impairment of the nutrition and of the elasticity of the lungs which occurs as a result of old age, anæmias and wasting diseases, and chronic lead-poisoning. There is not necessarily any element of increased intra-pulmonary pressure in its causation, though of course, this may be, and often is, also present.

Distribution of the change.—The commonest situations in which emphysema in the lung occurs are those which are least supported, for example, the anterior margins (especially on the left side, where the lung overlaps the pericardium), the anterior and posterior aspects of the lower margins, the right middle lobe, and the apices.

(*b*) " **Hypertrophous** " or " **Large-Lunged** " **Emphysema.**—This is always produced by physical conditions which lead to an **increased relative pressure** in the air-cavities and passages, as, for example, in forced expiratory efforts with the glottis closed or partially closed, or with the bronchi partially obstructed. Among the most potent factors producing this are the constant cough associated with chronic bronchitis, or repeated attacks of spasmodic asthma. Early rigidity of the chest-wall has also an important causal relation. The emphysema which occurs in young children is, by some authorities, regarded as hereditary—the elastic tissue in the lung, according to them, being very much diminished.

Nutritive disturbances, which are the main cause of the atrophous form, also have some share in the production of the hypertrophous type. The **distribution of the change** is similar to that seen in the atrophous form.

Morbid Anatomy.—The lung is usually very voluminous, the anterior margins meeting at, or even crossing, the middle line, and also overlapping the heart to an abnormal degree, in some cases covering completely the " bare area " of the pericardium. At parts, large, irregular, thin-walled, bullous projections may be seen. The tissue is extremely light, pale in colour and almost bloodless—the inter-lobular septa being
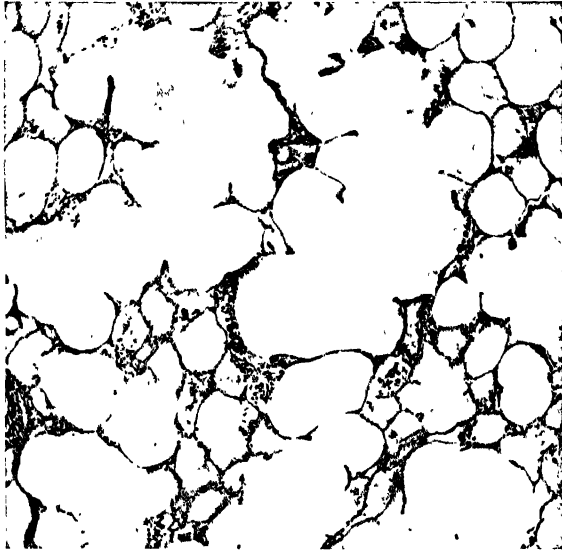
FIG. 306.—Emphysema of Lung, shewing distension of the air-vesicles, with thinning and atrophy of the inter-alveolar septa. × 50.

often mapped out by the presence of carbon-pigment. **On section,** the lung is dry, soft, and spongy, and the air can be readily moved from one air-space to another. **On microscopical examination,** the air-cavities are greatly distended, and their walls stretched and thinned. Partly on account of the stretching, and partly owing to an interference with their vascular supply, the inter-vesicular septa atrophy and give way, and intercommunication takes place between the adjacent air-spaces. The interlobular septa may shew thickening. The smaller branches of the pulmonary arteries may exhibit fibrosis, and the larger branches atheroma. The obstruction to the pulmonary circulation, due largely to the obliteration of the alveolar capillaries, causes dilatation and hypertrophy of the right ventricle and dilatation of the pulmonary artery. There is generally **associated chronic bronchitis,** which, though often the primary cause of

the emphysema, becomes exaggerated on account of the congestion produced in the bronchial walls by the dilatation of the collateral anastomosing vessels. These, in the attempt to compensate for the obstruction in the emphysematous parts of the lungs, establish increased communications between the pulmonary and the bronchial system of blood-vessels.

Ætiology.—As has been already stated, one of the main factors in the causation of emphysema is **forced expiratory effort** with the glottis closed. Increased pressure is thus produced in the air-vesicles and infundibular passages. This leads to their gradual distension, to pressure on their walls, and to narrowing or obliteration of the vessels in these walls. Thus, the septa have their blood-supply much impaired, and consequently undergo atrophy, and rupture. In addition, however, to this expiratory cause, **obstruction to the entrance of air** into one part of the lung leads to **increased inspiratory expanding force** in the neighbouring parts, with consequent distension of the air-spaces and the production of complementary emphysema. This inspiratory form occurs especially round collapsed or consolidated areas of lung-tissue. It is well illustrated in cases of lobular collapse in broncho-pneumonia, and also in spasmodic asthma.

INTERSTITIAL EMPHYSEMA.—In this somewhat rare condition, the air is found, either in the interstitial tissue of the lung alone, or it may, in addition, be widely spread in the cellular tissues of the mediastinum, neck, chest-wall, or even over almost the whole body. This form of emphysema may occur from rupture of the lung-tissue during an attack of whooping-cough, or as a result of great exertion, *e.g.* in the course of difficult labour. Sometimes, it results from the rupture of an emphysematous bulla, or from a wound of the lung, trachea, or bronchi. Thus, in laceration of the lung by a fractured rib, a varying degree of interstitial emphysema generally results. The condition may spread along the root of the lung to the cellular tissue of the mediastinum, root of the neck, etc.

Interstitial emphysema may be simulated *post mortem* by the presence of bubbles of gas found in the tissues of the lungs as a result of decomposition.

INFLAMMATORY CONDITIONS :—

(*a*) **ACUTE CONGESTION OR ACTIVE HYPERÆMIA** results from the action of bacterial and toxic irritants, and may be merely part of a general infection. In cases of lobar pneumonia, there is a preliminary stage of acute congestion, and this congestion may also occur in other toxic and septicæmic conditions, as, for example, in the acute infective fevers, etc., without necessarily being followed, as in the case of pneumonia, by consolidation. It is characterised by dilatation and engorgement of the alveolar capillaries, the walls of which, however, are

not thickened, as they are in chronic venous congestion. The alveolar spaces may be empty, or may contain, in varying proportions, blood, transuded lymph, or fibrin derived from these, and perhaps a few inflammatory cells.

(*b*) **ACUTE LOBAR PNEUMONIA (CROUPOUS OR FIBRINOUS PNEUMONIA)** is an acute infective disease, which some authors regard as **a septicæmia,** in which, for some unknown reason, the special local lesion is in the lung. Though it is true that the invasion of the lung is only one of many possible local manifestations of pneumococcal infection, and that the *Pneumococcus* may produce septicæmia without any true **pneumonia** and that, in cases of pneumonia, the organism is found, by cultural methods, to be present in varying numbers in the blood-stream, yet, the localisation of the disease is so frequent in the lung that most authors regard the lung as the primary seat of infection.

Ætiology.—The main causal factor of this disease is the *Diplococcus* or *Streptococcus pneumoniæ* (*Pneumococcus* of Fränkel). This organism is found in enormous numbers in the sputum and in the lungs, and is also present in the circulating blood. In a certain proportion (less than five per cent.) of cases, the *B. pneumoniæ* (*Pneumobacillus* of Friedländer) appears to be the cause. Other micro-organisms, *Staphylococci, Streptococci, B. influenzæ, B. pestis,* etc., seem capable of causing a very similar condition—either by themselves, or in association with the *Pneumococcus*—though they more commonly give rise to irregular patches of consolidation, which, however, may coalesce and produce an appearance simulating acute lobar pneumonia. In various epidemics of **infectious pneumonia** presenting both the lobar and the lobular type, *Streptococci* and *B. influenzæ* have been the main organisms found, and have been regarded as causal. There is also evidence that certain very acute and fatal cases, without much consolidation, have been associated with so-called **lymphatism,** and in these, *Pneumococci* have been found in considerable numbers. Recent work seems to show that the **type** of *Pneumococcus* varies in different cases, and that the pathological changes, the mortality, and the infective nature of the disease, are to some extent dependent on the type of organism concerned.

Certain predisposing factors, such as exposure to cold, fatigue, etc., have been long recognised by clinicians as aiding in the production of pneumonia. These cannot be overlooked, and must be regarded as important agents in preparing the soil for the growth and development of the causal organism—the *Pneumococcus* being, in comparatively non-virulent form, a common inhabitant of the mouth and throat.

Site of Origin and Mode of Spread.—There seems little doubt that acute lobar pneumonia commences generally near the root of the lung, and spreads, with a sharply defined margin, especially outwards and downwards in the lower lobe, or directly outwards to the middle lobe on the right side. There is a tendency for the disease to involve the

whole or **the greater part of one lobe,** hence the term **lobar** pneumonia applied to it, or the condition may spread more widely and involve **almost the whole lung.** It is not common to find two separate areas in the same lung affected, but both lungs may be involved, the latter condition being known as "double pneumonia."

Pathological Anatomy.—Typical cases pass through several distinct stages.

(i) **The stage of Acute Congestion.**—Reference has already been made to this. The affected area shews the ordinary phenomena of the early stages of acute inflammation, i. e. distension of the capillaries and venules, and exudation of lymph—the lymph in this instance passing
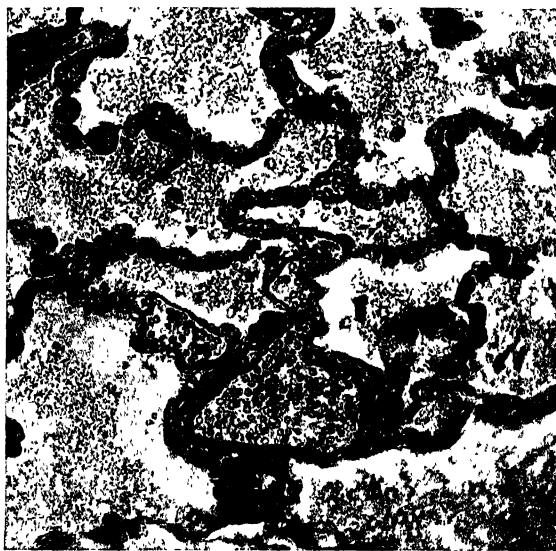
Fig. 307.—Acute Congestion of Lung, shewing dilatation of vessels in the alveolar walls and œdema in air-spaces.   ×200.

into the air-spaces, rendering the lung more or less solid, and producing a condition of **imflammatory œdema.** The epithelium lining the alveoli may shew swelling, or even proliferative changes, and a few leucocytes may have migrated from the distended vessels. Hæmorrhage into the alveoli may also occur during this stage.

(ii) **The stage of Red Hepatisation.**—This is merely a further stage of the acute inflammatory process. The **distension of the vessels** is very marked, the **exudation of lymph** persists, and, in addition, the **emigration of the leucocytes** has become pronounced. These leucocytes, which are mainly of the polymorphonuclear variety, pass in great numbers into the alveolar spaces, and, by their destruction, bring about the production of fibrin in the exuded lymph. Thus, the air-spaces become filled with fibrin and leucocytes, the air is driven out, and the lung becomes

consolidated and expanded—the consolidated lobe being often much increased in size. The epithelial cells lining the air-spaces undergo proliferation, and are found in the exudate as mononucleated phagocytic cells.

Naked-eye Appearance.—The affected lung, or part of it, is airless and solid, and, on the serous surface of this area, there may be an associated **acute pleurisy,** shewing itself either as a slightly granular-looking, sticky exudate or, more typically, as a thick, yellowish-white, soft and friable fibrino-purulent layer, which can be easily stripped from the surface. **On section,** the consolidated area has a bright-reddish or reddish-grey granite-like appearance, is very friable, more or less smooth and uniform,
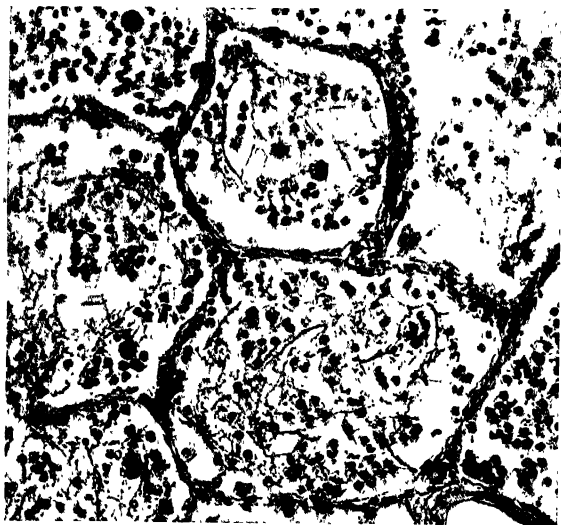
Fig. 308.—Acute Pneumonia, in the stage of red hepatisation. The air-spaces contain fibrin and leucocytes. × 200.

and stands above the general level of the non-consolidated tissue. The consolidation in lobar pneumonia produces an appearance resembling that of a solid organ such as the liver, hence the term " hepatisation " applied to it.

On microscopical examination, the appearances vary considerably. The **air-cells** are filled with fibrin, leucocytes, red blood-corpuscles, and mononucleated phagocytic cells, in varying proportions, and the walls of the alveoli are congested. The causal organisms may be found in enormous numbers in the exudate. The **fibrous septa** of the lung may be somewhat swollen and infiltrated with leucocytes; there is always an associated **acute bronchitis ;** and the **bronchial glands** are swollen, soft, congested, and sometimes œdematous. The microscopical changes in the pleura are described under **Diseases of the Pleura,** p. 725. (*See also* under **Inflammation,** Chapter VI.)

Results.—The condition may now, in favourable conditions, pass to the stage of **resolution,** to be described later, or, under less favourable circumstances, to the stage of **grey hepatisation.**

(iii) **The stage of Grey Hepatisation.**—In this stage, the lung remains solid, the congestion begins to pass off, and the cellular exudate tends to undergo degenerative changes. Thus, the lung is paler in colour, somewhat resembling grey granite, and, on **section,** appears finely granular owing to the exudate becoming loosened and lying more or less free in the air-cavities. The tissue is very friable, and a sticky semi-purulent fluid containing fine granules of fibrin may, on squeezing the lung, exude from
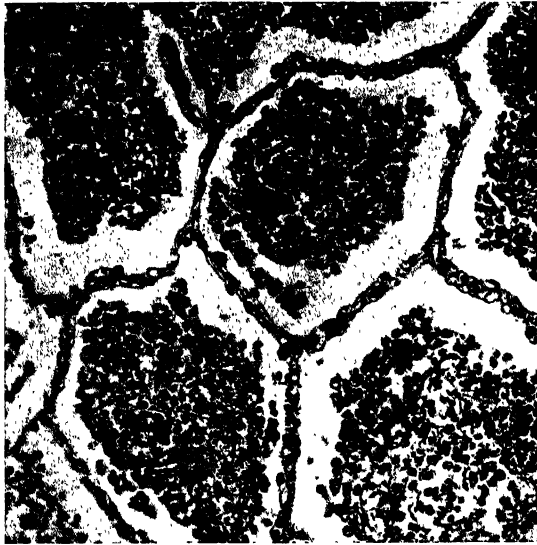
Fig. 309.—Acute Pneumonia, in the stage of grey hepatisation. The contents of the air-spaces are seen retracted from the alveolar walls. × 200.

the cut surface. **On microscopical examination,** the contents of the air-spaces are seen to be **retracted** from the walls, the cells and fibrin are still present, the polymorphonuclear cells are in greater numbers, and many of them exhibit karyolysis, karyorrhexis, and other degenerative changes. The mononucleated phagocytic cells, especially in the less serious cases, are increased in numbers at this stage. The congestion of the vessels in the inter-alveolar walls is much less marked, and may have completely passed off. Bronchitis is commonly seen in the smaller bronchi, whilst the exudate on the pleural surface may have become partially organised.

(iv) **Further changes which may occur in the consolidated lung :**

I. Under favourable conditions, the disease is arrested, and absorption of the inflammatory products takes place. This **stage of resolution** may follow those of acute congestion or red hepatisation, but it probably takes place much more rarely, if any marked degree of grey hepatisation

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has occurred. During resolution, the fibrin and other contents of the air-spaces become retracted and may be expectorated; but, more commonly, they undergo absorption by the aid of the mononucleated and other phagocytic cells. In some cases, especially in children, resolution is carried out almost wholly by the process of **absorption,** little or none of the exudate being expectorated as sputum. The cells lining the alveoli and the bronchioles proliferate and repair the damaged portions. Eventually, the lung may be completely restored to its normal condition.

II. In less favourable circumstances, the **resolution may be incomplete,** or **complications** of various kinds may arise. Thus—

(1) Areas of **softening** and of **suppuration** may appear, giving rise to **localised abscess-formation ;** or a more **diffuse suppurative condition** throughout the pneumonic area may supervene. This is not common, but may occur especially in cases of diabetes mellitus and in chronic alcoholism.

(2) **Gangrene of the lung** may result from the additional action of organisms causing putrefactive changes, and this condition is specially seen in cases of **pneumonia** occurring in patients who are suffering from diabetes mellitus or chronic alcoholism.

(3) **Chronic interstitial pneumonia** may be a sequel of imperfect resolution, and, associated with the resulting overgrowth of fibrous tissue, atrophy of the aërating tissue of the lung occurs. The contraction of the newly formed tissue may exercise traction upon the bronchi and give rise to dilatation of these—bronchiectasis. In certain rare cases, organisation of the intra-alveolar exudate may occur, capillaries and fibroblasts passing in from the walls.

(4) Rarely is there any considerable serous exudation into the pleural cavity, but the fibrinous exudate may soften and become purulent, giving rise to **empyema.** Such an empyema may be general, or localised by adhesions, e. g. between the lobes, or on the diaphragmatic, or on the outer, surface. As resolution proceeds, the pleural exudate undergoes organisation, and thus **adhesions** are formed between the visceral and the parietal pleura, and between the adjacent lobes. These adhesions may be very extensive, and the whole pleural cavity become obliterated.

(5) Pneumonia being an acute infective septicæmic disease, the pneumococci become lodged in situations other than the lung, and thus complications, such as **pericarditis, endocarditis, meningitis, peritonitis, arthritis,** etc., may arise.

(6) **Pericarditis** may arise also by direct spread from the lung, and a certain degree of **mediastinitis** is common.

The **toxins** act on the various organs, which may shew the changes—for example, cloudy swelling, fatty degeneration, etc.—generally seen in acute febrile diseases. A marked **inflammatory, polymorphonuclear,** or **neutrophil leucocytosis** is produced in the blood, as a result of

a **leucoblastic reaction in the bone-marrow.** In some cases, especially in chronic alcoholic patients, this reaction may not occur, the condition— a very grave and usually fatal one—being known as **pneumonia with leucopenia.**

The **sputum** in acute pneumonia is mucoid and abundant, and, very early in the disease, is blood-stained. It then becomes rusty-looking and very tenacious, and, in this stage, is characteristic. The colour is due to altered hæmoglobin. If there is much catarrh of the larger bronchi, mucopurulent masses are more or less abundant. Frequently, streaks of blood are seen, and sometimes the sputum consists of almost pure blood. Microscopically, various cells are found—polymorphonuclear leucocytes, epi- and endo-thelial cells, lymphocytes, etc. At the crisis, the sputum loses its rusty colour and becomes muco-purulent, and, later, consists mainly of whitish mucus.

A **greenish sputum,** in the absence of jaundice, is often an indication of suppurative changes or of tuberculous infection. Where necrosis or gangrene follows on pneumonia, the sputum becomes more fluid and assumes a **prune juice** or **chocolate** colour, and the odour is generally fœtid.

Branching fibrinous casts are often found.

(c) **ACUTE BRONCHO-PNEUMONIA (CATARRHAL or LOBULAR PNEUMONIA).**—This condition practically always commences as an inflammation in the smaller intra-lobular branches of the bronchi. The walls of these become congested, and this congestion spreads to the walls of the neighbouring air-cavities, into which hæmorrhage and some fibrinous exudation may occur. The affected bronchus or bronchiole becomes blocked with exudate and secretion, and, as a sequel, the portion of lung-tissue supplied by that bronchus or bronchiole undergoes collapse. The inflammatory process spreads, not only to the adjoining air-vesicles through the thin walls of the bronchus, but also along its interior to the collapsed area, which becomes the site of congestion, leucocyte-accumulation, fibrin-exudation, etc. In this manner, irregular consolidated areas of broncho-pneumonia are formed. Some of the neighbouring air-cavities undergo acute distension, as they receive more than their due share of the inspiratory distending force; and this distension, together probably with some direct weakening of the walls by inflammatory changes, leads to the characteristic areas of acutely produced **emphysema** which are seen around a broncho-pneumonic focus with collapse.

Causes of broncho-pneumonia.—In a large proportion of cases, the capillary bronchitis is produced by, or arises as a complication of, one of the acute infective fevers, such as measles, whooping-cough, diphtheria, influenza, smallpox, or typhoid and typhus fevers; and it is especially common in children. It may likewise result from the inhalation of irritant vapours or gases, and is a frequent complication in poisoning by chlorine, phosgene, or " mustard-gas." (*See* pp. 675–6.) The lodgment of irritant

particles of food, secretions, etc., also gives rise to broncho-pneumonia; but it will be more convenient to describe this form separately under the term "**Septic**" **Broncho-Pneumonia** (*see* p. 695). Sometimes, acute inflammatory changes in the lymphatics round a bronchus, as is seen in glanders and in influenza, may spread and involve the adjacent lung-tissue, and thus produce areas of broncho-pneumonia.

The **sputum** is usually muco-purulent, with portions of a rusty appearance, and sometimes streaked with blood. The cellular content is very similar to that found in the sputum of lobar pneumonia.

On bacteriological examination, *Pneumococci* and *Streptococci* are found in the great majority of these cases. Other organisms may occur either alone or in addition to these—for example, *Staphylococci*, *B. influenzæ*, *B. typhosus*, *B. pestis*, etc.

Naked-eye Characters.—These vary in different cases. The solid, airless nodules may be widely spread throughout the lung-tissue, or they may be more localised to certain parts of the organ. They may become confluent and thus involve large areas of lung-tissue. Being lobular—*i. e.* corresponding to lobules or groups of lobules—in their distribution, they are more or less polygonal in shape; and are of a slaty-blue or reddish colour. On section, there is usually a darker-reddish central part, corresponding to the area of congestion round the bronchiole; or the centre may become pale and greyish on account of the accumulation in it of emigrated and degenerating cells. On compressing the lung, little points of yellowish-white muco-pus exude from the smaller bronchi, some of which shew acute dilatation of their lumen. The areas of consolidation may be slightly raised above the general surface of the lung, and are commonly surrounded by a zone of acute emphysema. When the broncho-pneumonic areas are numerous, they tend to coalesce, the intervening lung-tissue becomes œdematous and congested, and the appearance produced comes to resemble that of acute lobar pneumonia. Such "pseudo-lobar" spread is specially common in influenzal cases. Usually, however, the section has a somewhat marbled appearance, from the patches being scattered and at different stages of the inflammatory process.

Microscopical Appearances.—In the areas of consolidation, the corresponding intra-lobular bronchus shews very definite catarrhal changes, and frequently marked dilatation. The vessels in its walls are congested, and the lumen is filled with exudate containing desquamated epithelium, leucocytes, mucoid secretion, granular débris, etc. The neighbouring air-vesicles are consolidated, the cavities being crowded with cells of various kinds, those next the bronchi usually containing, in addition, fibrin. The cells in the alveoli may be grouped as follows :—

(1) **Red blood-corpuscles.**—These may be very numerous in the more intense hæmorrhagic forms of the disease.

(2) **Large mononucleated cells.**—Some of these are probably derived

Fig. 310.—*Lung.* Shewing large areas (pale) of broncho-pneumonia, from a case of bubonic and pneumonic plague.

Fig. 311.—*Lung.* Shewing the "infarct-like" areas of broncho-pneumonia, from a case of bubonic and pneumonic plague. (Semi-diagrammatic drawing from a fresh specimen.)

from the blood, but others are the proliferated and desquamated cells of the lining endothelium of the alveoli.

(3) **Polymorphonuclear leucocytes.**—These vary in number, the variation being dependent on the nature and intensity of the irritant, and on the duration of its application. Thus, infection with *Pneumococci*, *Streptococci*, or *Staphylococci* will call forth large numbers of the polymorphonuclear variety of cells; whilst, in the case of *B. typhosus*, the mononucleated cells will be more abundant. At the early stages of the inflammatory process, in uncomplicated cases, the polymorphonuclear variety is more abundant than in the later stages. In very serious; and especially in fatal, cases, the increase in the polymorphonuclear leucocytes
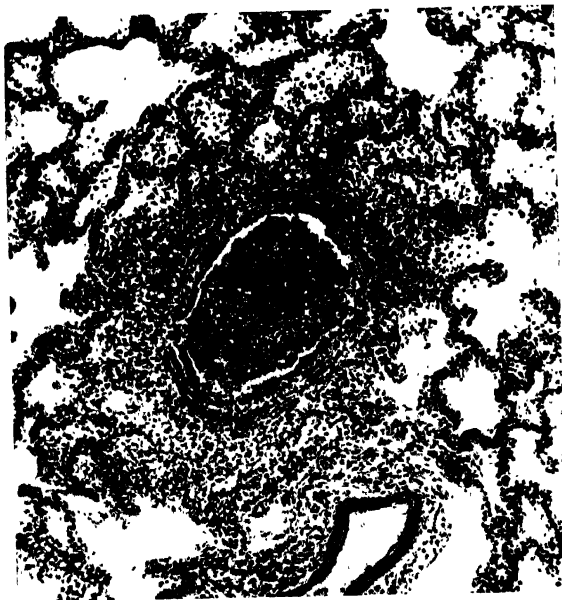
Fig. 312.—*Lung.* Showing an area of broncho-pneumonia. The lumen of the bronchiole is filled with inflammatory exudate, and there is consolidation of the surrounding air-spaces. 75.

is maintained throughout, and actual suppuration may result. The causal organisms can usually be demonstrated with suitable stains.

(4) **Columnar and ciliated cells** inhaled from the bronchioles may sometimes be present.

(5) Occasionally, foreign **vegetable or other cells,** derived from the inhalation of particles of food, are found in the small bronchi. These may, in some cases, be the exciting cause of the broncho-pneumonia, but, more commonly, they are the result of inspiratory efforts in the last stages of life.

Associated with the consolidation are areas of **collapse** and of **emphysema, exhibiting** the usual microscopical appearances of these conditions.

The intervening lung-tissue may shew **intense congestion** and **œdema,** the **inter-lobular septa** be swollen and œdematous, and evidence of **acute pleurisy** be seen over the nodules immediately subjacent to the surface of the lung.

Subsequent Changes.—The inflammatory products may be absorbed or expectorated, and the lung may return to its normal condition. In some cases, however, the collapsed portions remain uninflated, and shrinking and deformity of the lung-tissue result. Or again, the catarrhal condition sometimes becomes **chronic,** and an **interstitial pneumonia** may develop—the new tissue encroaching upon, and obliterating, the alveoli. Thickening of the tissues round the minute bronchi and dilatation of the latter are not uncommon, especially in children; and, in the affected area of lung, numerous bronchiectatic cavities, resulting from the dilatation, and usually comparatively small in size, are frequently seen. Thickening of the inter-lobular septa also occurs. The areas may become infected with *B. tuberculosis,* and, in such cases, certain characteristic changes are observed, which will be discussed under **tuberculous broncho-pneumonia. Suppuration** and **gangrene** may result, and these depend, to a certain extent, on the character and virulence of the causal organism. Thus, in cases caused by the *Staphylococci,* suppuration is commoner than in those which arise from infection with the *Pneumococcus.* More frequently, however, the suppuration is due to a mixed infection. A more or less widely-diffused purulent infiltration may occur in streptococcal cases.

(*d*) " **SEPTIC** " **BRONCHO-PNEUMONIA.** —This term, though not a very satisfactory one, is applied to a form of broncho-pneumonia which, in its histological features, resembles the form of lobular pneumonia above described, but which shews a marked tendency to the occurrence of **suppuration.** It is generally due to the inhalation into the finer bronchi of foreign, and, especially, of decomposing, material. It occurs as **vagus-pneumonia,** where—owing to interference with the vagus or the recurrent laryngeal nerve, and consequent paralysis of the muscles which close the glottis—food gains entrance into the bronchi : as **aspiration-pneumonia,** where secretions from the mouth or the larger air-passages are drawn into the finer bronchi : or as **retention-pneumonia,** where, from pressure upon, or obstruction of, a bronchus by an aneurism or a tumour, by syphilitic stenosis, or by inhalation of a foreign body, *e. g.* a tooth which has been inhaled during extraction under an anæsthetic, the secretion is retained in the bronchial passages. The food or other foreign body, or the retained secretion, sets up irritative changes in the bronchi, which render them more liable to invasion by bacteria. Catarrh and ulceration, and subsequently—from a spread of the inflammatory processes to the neighbouring lung-tissue—consolidated areas of broncho-pneumonia, are produced. Minute points of pus, which look like multiple abscesses,

are seen in these areas; and, on careful examination, these are found to be dilated and ulcerated bronchi, filled with purulent secretion. More extensive abscess-formation frequently occurs, and the abscesses, if on the surface, may lead to the production of pleurisy, or may burst into the pleura and give rise to empyema. In these cases of **aspiration-pneumonia,** a very considerable overgrowth of fibrous tissue, producing a condition of chronic interstitial pneumonia, sometimes supervenes.

(*e*) **ABSCESS OF THE LUNG.**—As already stated, the consolidated areas of septic broncho-pneumonia may become softened and purulent, but abscess-formation is in most cases a manifestation of **pyæmic infection,** though it may occur round a foreign body. It sometimes occurs in **puerperal septicæmia, suppurative periostitis, osteomyelitis, middle-ear disease with thrombosis of the lateral sinus,** etc. The micro-organisms are carried to the lung directly in the blood, or by means of emboli from a preliminary malignant endocarditis of the pulmonary or tricuspid valves. Embolism and thrombosis of small branches of the pulmonary artery follow, and irregular areas, which, at first, correspond with hæmorrhagic infarcts, are produced. These soon become greyish or yellowish in colour, soften, and break down into irregular suppurative cavities. The tissue round the abscess is intensely congested and œdematous, and is often also hæmorrhagic. **Microscopically,** the condition is seen to be a hæmorrhagic catarrhal pneumonia in which suppuration supervenes. The abscesses are usually multiple, vary considerably in size, from very minute points of suppuration to large abscesses, and the pleura over them may shew acute inflammatory changes. Rupture into the pleural sacs, giving rise to empyema, or more commonly to a pyo-pneumothorax, may take place, or the abscess-cavity may burst into the bronchi. **Greenish-yellow pus,** often in considerable amount, and containing fragments of lung-tissue, is a constituent of the **sputum** in such cases.

GANGRENE OF THE LUNG :—

This condition always results from the action of putrefactive organisms upon damaged or dead lung-tissue. It may be due to the direct extension into the lung of necrotic and ulcerating areas in the œsophagus, in the stomach, or in the bones of the chest-wall: to putrefactive material inhaled from ulcerative and necrotic processes in the upper air-passages : or to putrefactive changes in the secretion which accumulates in the bronchi, as a result of obstruction by the pressure of tumours or aneurisms. In other instances, it seems certain that the infective material reaches the affected area by the blood; but probably, in these instances, the organisms introduced are causal of this condition simply because they have tissues, already damaged and devitalised, on which to act. The gangrene which sometimes follows pneumonia seems to be due to the

Pneumococcus—alone, or in conjunction with other organisms of secondary infection—acting on specially damaged tissues.

There are also certain **predisposing factors.** Thus, in diabetes mellitus and in chronic alcoholism, pneumonia not uncommonly terminates in gangrene.

Morbid Anatomy.—The gangrenous area is soft and putty-like, and usually has a very foul odour. It may be dark reddish or greenish, or almost black in colour. The surrounding tissue is intensely congested, it may be consolidated, and is often extremely œdematous. The condition may be localised, or it may be widely spread. Communications with the bronchi are common, and the expectoration is profuse, muco-purulent, of a yellowish or brownish colour, generally intensely fœtid, and may contain shreds of necrotic lung-tissue, alveolar epithelium, often with included pigment, fatty-acid crystals, and fat-droplets. Masses of various kinds of bacteria, including leptothrix filaments, are found. In some cases, where death does not occur, the whole of the gangrenous contents are discharged through the bronchi, and the cavity may become gradually filled by granulation-tissue. Thus, repair is effected, and, at a later period, an irregular scar is the only sign of the original gangrenous area.

HYPOSTATIC PNEUMONIA :—

Reference has already been made to the condition of **hypostatic congestion** and **œdema** of the dependent parts of the lungs (*see* p. 679). These conditions may pass to the stage of **consolidation.** A subacute form of inflammation of the terminal bronchioles and air-vesicles is set up, and, in this way, the cavities become filled with catarrhal cells and with fibrin and leucocytes.

INTERSTITIAL PNEUMONIA :—

Interstitial Pneumonia is generally a subacute or chronic condition which results from continued irritation, and may involve larger or smaller areas of lung-tissue. It is, however, sometimes acute, as in some cases of influenza, and it then resembles the " pleuro-pneumonia " of cattle.

The condition, in its subacute and chronic manifestations, is characterised by an overgrowth of the connective-tissue framework of the lung, and this may give rise to secondary changes in the bronchi, lung-tissue, vessels, etc.

Classification.—Of these subacute and chronic forms, several varieties, the special characters of which are largely dependent upon the different causal factors at work, have been described. The most important are—

(1) Those resulting from the **inhalation of dust** or other foreign particles (the **Pneumonokonioses**). The most familiar examples are the conditions produced by the irritation of coal- or stone-particles, in coal-miners, stone-cutters, and grinders.

(2) Those which **follow acute or subacute conditions** of the lung or pleura, as, for example, imperfectly resolved acute lobar or lobular pneumonia, collapse, irritation of a foreign body, vagus- and retention-pneumonia, pleurisy, etc.

(3) Those which are the result of the action of **bacterial and other organismal poisons.** Of these, the most important are the interstitial pneumonias of tuberculosis, syphilis, leprosy, glanders, and influenza.

Microscopical Anatomy.—The different varieties of interstitial pneumonia present certain common features. The **connective-tissue overgrowth** always commences in positions in which the original connective tissue
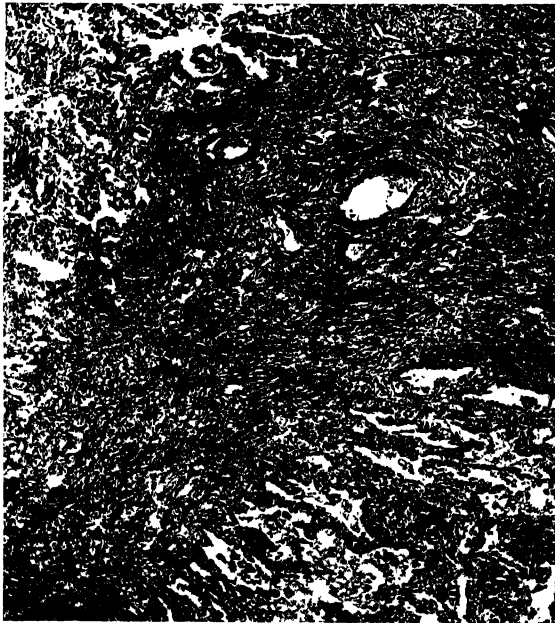
Fig. 313.—*Lung.* Interstitial Pneumonia, shewing great increase in dense fibrous tissue, and also the " pseudo-glandular " character assumed by the alveoli. × 50.

is most abundant, and gradually invades the lung, encroaching upon, altering, and obliterating the aërating tissue. During the progress of this invasion, the endothelium lining the alveoli becomes altered in character. The cells are more cubical or spheroidal, and simulate those of gland-tissue or of the embryonic lung. The walls of the alveoli come in contact, and, gradually, obliteration takes place. This alteration of the endothelium may be seen in any of the forms of interstitial pneumonia, and is really a stage in the obliteration of the alveoli, but it is, perhaps, best seen in the variety due to syphilis. This cubical or columnar type of endothelium may be very abundant, and the appearance produced may easily be confused with that seen in adenoid cancer of the lung. The starting-points for the overgrowth of connective tissue are most

commonly the deeper layer of the pleura, the inter-lobular septa, and the connective tissue round the bronchi and the vessels. In the varieties which occur in influenza and in glanders, it is the peribronchial and the perivascular tissues which show special proliferative changes; whereas, in the forms due to dust-diseases, the main change seems to be in the deep layer of the pleura and in the inter-lobular septa.

The proliferated connective tissue varies in its character in the different forms. It may be very dense and shew little evidence of cellular growth, or the cellular character may be extremely marked. The degree of vascularity also varies very considerably. The bronchi may become dilated during the more acute stage, and this dilatation may persist, or even be increased later. The secretion may be retained, undergo decomposition, and cause still further dilatation and the production of a condition of **bronchiectasis.** The invading fibrous tissue may cause the obliteration of large tracts of the smaller bronchi. The fibrous nodules thus formed shew a dense, homogeneous, central fibrous zone surrounded by pigment, this pigment mapping out the position of the peribronchial lymphatics.

1. THE PNEUMONOKONIOSES.—The results of the inhalation of dust depend largely on the character of the particles inhaled. Thus, that part of the fine dust of the air which is not expectorated, is taken up from the channels and cavities of the lung into the lymphatics, and is deposited in different situations, but does not necessarily give rise to any serious damage. If the dust, however, is of a specially irritating character, it acts as a foreign body in the positions in which it is deposited (the **deeper layer of the pleura,** the **inter-lobular** and **inter-alveolar septa,** and the **peribronchial** and **perivascular lymphatics**), and causes chronic irritative changes, with the production of nodules of fibrous tissue.

According to the character of the dust inhaled, various names have been given to the lesions produced.

(a) **ANTHRACOSIS** (" **COAL-MINERS' LUNG** ") is due to the inhalation of particles of coal, shale, soot, or other forms of carbon. The dust here is not physically very irritating, and, in consequence, the nodules of fibrous tissue are, as a rule, small, though usually widely distributed.

The lung becomes intensely black, and the pleural surface usually shews some small, irregular, white, fibrous areas, surrounded by a darker zone of pigment. Under these fibrous areas, gritty particles may be felt. The cut surface is also finely gritty.

On microscopical examination, large masses of black pigment, in the form of fine granules, are seen in the connective tissue, which is often almost obscured by them. The bronchi and air-cells generally shew catarrh, and the lung-tissue may be congested and emphysematous. Many of the catarrhal cells contain granules of the pigment.

(b) SILICOSIS (CHALICOSIS or "STONE-MASONS' LUNG") is due to the inhalation of stone-particles, or particles of glass or quartz. Only certain kinds of stone produce the irritation, especially those containing high percentages of silica, such as granite, flint, etc. The fibrous nodules formed, in this condition, are usually fewer in number than in anthracosis, and, on account of the extremely irritating nature of the particles, they are larger and denser in consistence. Destructive changes are also more marked. The central part of the nodules often shews necrosis, owing to the obliteration of the vessels at the periphery by the dense fibrous tissue.

On naked-eye examination, the lung has a greyish.colour. On the pleura, the whitish fibrous nodules, to which reference has already been made under anthracosis, are much more marked, larger, and more numerous. On section, the gritty stone-particles can be felt under the finger; and are seen to be surrounded by pigmented fibrous tissue.

On microscopical examination, dense nodules of fibrous tissue are seen, often homogeneous and necrotic in the centre, and containing minute angular or irregular masses of a greyish-black colour — the stone-particles. Catarrh, congestion, and emphysema of

FIG. 314.—Lung. Anthracosis, a characteristic example of "coal-miners' lung." (Edinburgh University Anatomical Museum. Catalogue No., R. C. a. 4.)

the intervening lung-tissue are commonly present. The vessels at the periphery of the nodules may shew obliterative endarteritis, and the connective tissue in this situation is more cellular and more vascular

Fig. 315.—*Lung.* From a case of Anthracosis. shewing the great accumulation of carbon-pigment. ×40.

Fig. 316.—*Lung.* From a case of Silicosis, shewing a dense, fibrous, and pigmented nodule. ×35.

than in other parts of the lung. **Tuberculosis** *is very frequently* associated with silicosis, and the destructive changes in such cases may be very marked.

(c) **SIDEROSIS (" GRINDERS' " or " TURNERS' LUNG," etc.)** is due to the irritation of metal-dusts and the dust from the grindstone— the latter being the most important factor in so-called " **Grinders' phthisis.**" Most authors lay stress on the damage done by iron- and steel-particles in the lungs of needle-grinders, file-makers, knife-grinders, etc. This view, which has been handed down in various textbooks, has very little evidence to support it. The experience of one of us among the grinders in Sheffield is that it is a **silicosis,** and not a siderosis, from which these workers suffer—it is the stone-dust, and not the iron or steel, that is the causal agent. The changes produced are identical with those seen in silicosis. Tuberculosis is a very common complication in the grinders' lung, at any rate in Sheffield, and, in the majority of cases, it is the cause of death. A definite interstitial pneumonia, however, undoubtedly does occur in grinders' lungs apart from tuberculosis, and there is no evidence that the silicosis is in itself a cause of phthisis (chronic pulmonary tuberculosis).

(d) **WORKERS WITH FLAX, FEATHERS, CLAY, PORCELAIN, PLASTERS, PIGMENTS,** etc., are said to develop a varying degree of interstitial pneumonia, but, in many of these workers, the changes are slight and unimportant, whereas in others, such as potters, the changes are really due to such irritating dust as flint or silica in some combination.

2. THE FORMS OF INTERSTITIAL PNEUMONIA WHICH FOLLOW ACUTE OR SUBACUTE CONDITIONS OF THE LUNG.—In these conditions, the fibrous overgrowth may occur in localised patches, or may be widely spread throughout the lung—the new fibrous tissue spreading inwards from the pleura, from the septa, or from the peribronchial and perivascular connective tissues.

3. THE FORMS OF INTERSTITIAL PNEUMONIA WHICH RESULT FROM THE ACTION OF BACTERIAL AND OTHER POISONS OR TOXINS.—Occasionally, an **acute interstitial pneumonia** resembling the pleuro-pneumonia of cattle is seen. In this, the principal change is in the inter-lobular septa, which become thickened, and from which extension takes place into the lung-tissue. Usually, there is also an associated peribronchitis.

This condition is seen specially in some of the cases of pneumonia which are associated with influenza. The more usual conditions resulting from the action of organismal poisons are those seen in syphilis and in tuberculosis; and these will be discussed under syphilitic and tuberculous disease of the lung.

SYPHILIS OF THE LUNGS:—

Syphilitic disease of the lungs may occur in either the **congenital** or the **acquired** form of the disease.

In the **congenital form, gummata** may be found, but the most characteristic change is an **interstitial pneumonia.** The lung is usually pale in colour and tough, and is intersected by delicate fibrous bands. This change, **white hepatisation,** or **white pneumonia** as it is sometimes called,

Fig. 317.—*Lung.* Syphilitic interstitial pneumonia. Stained for elastic tissue. × 28. Note obliterative endarteritis in vessel.

may be widely spread, or it may be confined to a small portion of the lung.

Microscopically, the connective-tissue overgrowth is, at first, very cellular and vascular, but, later, it may become more densely fibrous. The alveoli undergo compression, their walls are invaded by fibrous tissue, and the lining-cells become cubical or spheroidal. As the overgrowth continues, the vesicles become more and more collapsed, and various secondary changes, such as atrophy and obliteration, result.

In **acquired syphilis, gummata** are found, and are often surrounded by well-formed fibrous tissue. This tissue may contract, and the gummata

be absorbed; and thus irregular **cicatrices** may be produced. These are most frequently seen in the posterior and outer parts of the lower lobes.

Interstitial overgrowth, similar to that seen in congenital cases, may occur. *The fibrous tissue is, however, much less cellular. The fibrous bands which intersect the lung-tissue are situated usually at the posterior or outer aspect of the lower lobes, where they pass from the pleura inwards, and may be traced to, and be continuous with, the sheaths of some of the larger bronchi. By their contraction, very irregular and deep puckered* **cicatrices** *may be produced on the surface. In these fibrous bands, gummata or their remains may sometimes be found.* In some cases with syphilitic ulceration or stenosis of the larynx, the retained secretion may give rise to **retention-pneumonia** and to **bronchiectasis,** and **diffuse syphilitic interstitial pneumonia** may eventually result. Not uncommonly, secondary infection with *B. tuberculosis* and other organisms occurs.

In **GLANDERS** and in **ACTINOMYCOSIS,** a fibrous overgrowth may take place in the lung, though the more usual lesions are softening and abscess-formation. In **actinomycosis,** the fibrous tissue, which is really the scar-tissue of the healed abscess, may occur at any part of the lung; but, in glanders, the new tissue generally arises by a proliferation of the peribronchial and the perivascular connective tissues. Other **strepto-tricheæ,** *e. g. S. asteroides* (*Eppinger*), sometimes produce minute abscesses scattered throughout one or both lungs, and simulate acute miliary tuberculosis.

TUBERCULOUS DISEASE OF THE LUNGS AND PLEURA

Tuberculosis in the lungs may be part of a general process, or it may be localised in the lungs. All forms are primarily caused by the presence of B. tuberculosis; and the differences in the lesions depend on various factors, such as the **channel of infection,** the **method of spread in the lung** and the **special structures involved,** the **virulence of the organism** and the **power of resistance of the patient,** the presence or absence of previous disease and damage in the lung, and the supervention of intercurrent processes, especially secondary infection with other organisms.

CLASSIFICATION :—

(A) TUBERCULOSIS, WITHOUT CAVITY-FORMATION.

  I. **ACUTE :**

   1. **Infection by Blood-Stream**   . . . . ⎫ **Acute**
            ⎧ **Diffuse or** ⎪ **miliary.**
            ⎪ **scattered.** ⎭

   2. **Infection by Lymphatics**
            ⎪ **Localised Peri-**
            ⎩ **bronchial.**

   3. **Infection by way of the Air-Passages.**- -This usually gives rise to **acute caseating tuberculous broncho-pneumonia.**

  II. **CHRONIC.**- -This form is chiefly due to spread by the **peribronchial lymphatics.**

(B) TUBERCULOSIS WITH CAVITY-FORMATION (PHTHISIS).

  I. **ACUTE :** which is mainly **broncho-pneumonic** in type.

  II. **CHRONIC :** which is mainly seen in the **peribronchial lymphatics.**

GENERAL FACTS IN RELATION TO TUBERCULOSIS OF THE LUNGS :—

1. There is great variety in the rapidity, *i. e.* the acuteness or the chronicity, of the process, and, therefore, in the resulting lesions. Thus, the more acute the condition is, the greater is the tendency to **caseation and destruction,** the more chronic, the greater the amount of **fibrous-tissue overgrowth.** The appearances in the lung during the course of the disease depend largely on the relative proportion of these two changes to one another.

2. Tuberculous lesions in the lung may be part of a **general tuberculous infection** throughout the body, as, for example, in the acute miliary tuberculosis produced by inoculating animals : or that found in children, or in older patients with weak resisting power. On the other hand, the condition may **start in the lungs,** and from them the infection may be

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. carried to other parts of the body; or the lung may become infected from some other neighbouring focus of the disease.

3. In the lung, the lesion is **localised** or **diffuse,** and, *clinically,* seems specially to attack the apex of the right lung, though this is probably *due, as may be seen on post-mortem* examination, to an extension of the tuberculous process **from the root** of the lung. One lung is seldom affected alone, though it may appear to be so clinically. **Both** organs are almost always attacked, even early in the course of the disease, which is frequently more pronounced on one side, more especially the right.

4. Lesions resulting from other diseases may modify the changes—*e.g.* Silicosis, etc. (*q.v.,* p. 700).

5. When *B. tuberculosis* has once settled down, it tends—unless a cure is effected—to spread and cause more widely diffused changes.

METHOD OF INFECTION :—

Whitla,[1] in his Cavendish Lecture, revived the view of Calmette and others "that the immense majority of cases of pulmonary tuberculosis is *not* contracted by inhalation, but by the ingestion of bacilli or bacilliferous products which penetrate the intestinal mucosa." He and Symmers, from their experiments, conclude that : " carbon particles, china ink and *B. tuberculosis* pass through the intestinal epithelial surface, reaching the lacteal or lymphatic paths, then pass through the lymphatic glands of the mesentery, and finally, either enclosed in phagocytes or free, find their way into the thoracic duct, to be poured into the . venous circulation before being arrested in the capillaries of the lung." Though we are not prepared to accept these views for the majority of cases, and much evidence has been brought forward against them, there seems little doubt that one of the principal channels of entrance for the bacilli is the lymphatic one.

There is also a general agreement that one of the commonest channels of entrance in young children, is by way of the **tonsils** (including also the lymphoid tissue of the pharynx, etc.), and, in some cases, by way of the nose or teeth. From these situations, the bacilli pass to the **cervical glands,** then to the **mediastinal** and **bronchial glands,** and finally into the lung-tissue, especially by way of the **peribronchial lymphatics** of the larger bronchi.

From the root of the lung, the paths of infection may be—

(*a*) **Outwards and upwards,** involving the inner part and apex of the upper lobe.

(*b*) **Directly outwards** towards the axilla, *i. e.* to the middle part of the upper lobe, passing, in some cases, to the surface and infecting the pleura, causing tuberculous pleurisy, and sometimes leading to widespread re-infection of the lung by way of the sub-pleural and inter-lobular lymphatics.

[1] *Brit. Med. Jour.,* July 11, 1908, p. 61,

(c) **Outwards and downwards** into the lower lobe. This direction of spread, however, is brought about by an air-passage involvement from the inspiration of infected sputum along the bronchi.

The bacilli may also enter the lungs by way of **the pleura,** which has become invaded through the lymphatics in the diaphragm in cases of *abdominal tuberculosis. The right lung is more especially attacked in this way, the bacilli passing through the lymphatics of the right side of the diaphragm.*

If the **larger bronchi** become involved, the bacilli may pass along the peribronchial lymphatics directly to the lung, or may spread to the mediastinal, and then to the bronchial, glands, from which a peribronchial lymphatic re-infection of the lung may occur.

Invasion frequently takes place by way of the **intestine** and the **mesenteric glands.** In most cases, the intestine is ulcerated, but sometimes the bacilli pass through the intestine to the mesenteric glands without the intestine itself becoming involved. This condition is found usually in children, and, like the cervical form of the disease, is, in most cases, caused by the **bovine** type of bacillus. From the **mesenteric** glands, the bacilli may spread by way of the **retroperitoneal** and **mediastinal** glands around the aorta to the **bronchial** glands and to the lungs.

Infection by the Air-Passages.—This method of onset is also of frequent occurrence, and, in adults, it is probably the usual channel of infection. *B. tuberculosis* may be inhaled in dried-up sputum, infected dust, etc., and may be arrested in the moist walls of the nose, pharynx, trachea, or larger bronchi, and, from the last-mentioned structures, it may be carried to other parts of the lung by the lymphatics. It is possible—but probably not at all common—that the bacilli are originally carried further into the lung by the air-stream. The usual mode of spread into the smaller bronchi and air-cells—when it does occur—is by the inhalation into them of broken-down material from a tuberculous focus in the bronchi or in some other part of the lung, or by the inspiration, after hæmoptysis, of blood containing bacilli, *i. e.* it is a secondary and not a primary mode of infection.

SPREAD OF THE PROCESS IN THE LUNG ITSELF :—

The special structures which are affected in the lungs, and the character of the lesion, will depend largely on the special **channel of invasion,** as will also, to a large extent, the **nature and method of spread of the process** after it has once started.

The chief methods of spread are—

1. **By the blood-stream.**

2. **By the lymphatics** in the connective tissue.

    (a) The more general, diffusely or irregularly distributed lymphatic channels in the deeper layer of the pleura, the septa,

the peribronchial and perivascular tissues, and in the walls of the alveoli.

(b) The peribronchial lymphatics.

3. By the air-passages.
4. Local spread by infiltration.

Very frequently **several** of these methods of spread may be seen in the same case.

A.—TUBERCULOSIS WITHOUT CAVITY-FORMATION :

I. ACUTE TUBERCULOSIS

1. Blood Spread :—

An **embolic** or **arterial spread,** though of comparatively infrequent occurrence, produces one form of acute miliary tuberculosis. The bacilli may be carried to, and settle down in, the terminal branches of the pulmonary artery. This, however, is only part of a general tuberculous infection throughout the body. The original focus is frequently in the abdomen. The **bronchial glands** are enlarged, softened, and caseous; the **pleura** is studded with miliary tubercles; and the **lung** shews, on section, innumerable minute **tubercle-granulations** throughout its substance. There are usually, in addition, considerable **engorgement,** and **œdema,** and sometimes **pneumonic consolidation,** of the intervening lung-tissue.

2. Lymphatic Spread :—

The spread by lymphatics may shew itself in two forms :

(a) **The irregular, diffuse, or scattered form,** which is seen especially in very acute and rapid cases, occurring secondarily to disease of the pleura or of the glands at the root of the lung. The lesions produced in this form of **acute miliary tuberculosis** generally cannot be distinguished from those in the acute form which is spread by the blood-stream.

Naked-eye Appearance.—Large numbers of minute greyish nodules are seen scattered throughout the connective-tissue framework of the lung. They are irregularly rounded, often somewhat yellowish in the centre, and firm to the touch. They are also seen immediately under the pleura, and are distinctly raised above the pleural surface.

Microscopically, in their early stages, they are composed largely of lymphoid cells. There may be slight proliferation of the connective-tissue corpuscles and other cells, and the formation of so-called epithelioid, or, more correctly, endothelioid, cells, and slight evidence of central caseation may be seen. Usually, giant-cells are not formed. The walls of the alveoli may be thickened, and these, and the smaller bronchi, may be invaded by the tuberculous process. In this way, collapse and local catarrh may be brought about.

(b) **The more regular and localised form of spread,** by way of the peribronchial lymphatics, is seen in the less acute and in the chronic

manifestations of the disease; but it may occur in cases which develop very rapidly.

The character of the lesion varies with the size of the bronchus involved. The **walls of the larger bronchi** may be infiltrated to such an extent that
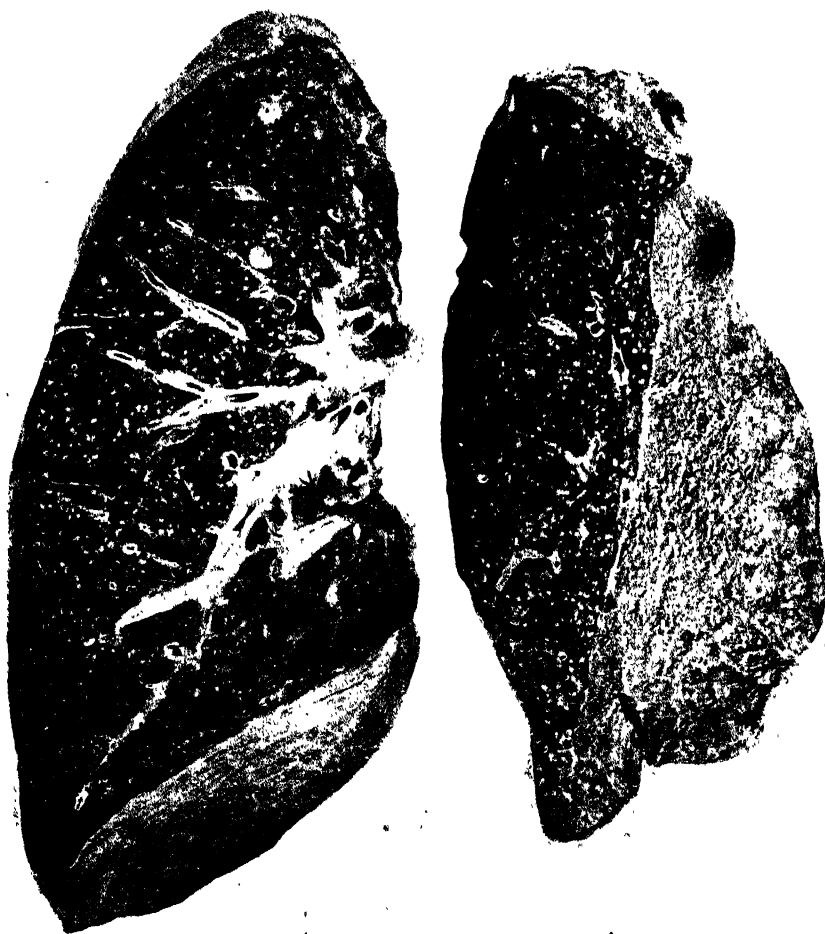
FIG. 318.—*Lung.*   Acute Miliary Tuberculosis.   Note tubercle-granulations on the pleural surface of right-hand figure.

the tube itself is narrowed and obstructed; or the tuberculous focus may ulcerate into the bronchus.   In either case, secondary dilatation and the formation of bronchiectatic cavities may occur, an acute tuberculous bronchitis being set up, and thus leading to a spread by the air-passages, and producing a tuberculous broncho-pneumonia.

Or again, the tuberculous infiltration may spread along the peri-

bronchial lymphatics to the walls of the smaller bronchi leading to one lobule or to a group of lobules, and there give rise to a similar reaction.

The tubercles become arranged in a racemose or staphyloid manner, corresponding to the divisions of the affected bronchus (*see* fig. 319). Ulceration into the bronchus may take place, or the lumen may be blocked by exudate, leading to obstruction and collapse, and then to tuberculous invasion and caseation of the collapsed area.

When the walls of the more **minute bronchioles** become affected, the lesion tends to invade the alveoli and to give rise to a condition of tuberculous bronchopneumonia.

3. **Air-Passage Spread :—**

This form of spread gives rise usually to the **catarrhal or broncho-pneumonic form of tuberculosis.** It is a frequent mode of secondary acute infection in the course of the more chronic cases, and is the elementary anatomical lesion in **acute phthisis** (*see* p. 716).

Methods of Infection.— The air-passages may become involved in the tuberculous process by the inhalation of contaminated dust from outside, or of secretions of blood which contain the bacilli from the air-passages or the lung itself. Such an infection may

Fig. 319.—*Lung.* Subacute Tuberculosis with some fibrous overgrowth towards upper part of lobe, and shewing acute peribronchial spread into the lower lobe. (Edinburgh University Anatomical Museum. Catalogue No., R. C. e. 6.)

arise also by the ulceration into the alveoli or into the bronchi of a tuberculous focus situated either in the peribronchial tissues or in the glands at the root of the lung.

Characters of the Lesions.—*The infective material produces in the minute bronchioles an intense catarrh, which spreads into the air-cavities.* This catarrh is associated with rapid necrosis and caseation, not only of the inflammatory products, but also of the walls of the small bronchioles, the alveolar passages, and the air-cells. The condition may affect a part, or the whole, of one lobule, or a group of lobules, according to the size of the bronchiole primarily involved. The walls of the air-spaces may be infiltrated with cells of a lymphoid type, and these cells may give rise to compression and to obliteration of the alveolar capillaries. Giant-cells are usually scanty or entirely absent, or they may be found only in the peribronchial tissue in the original tuberculous focus. The **intervening lung-tissue** may be intensely congested, may be œdematous, or
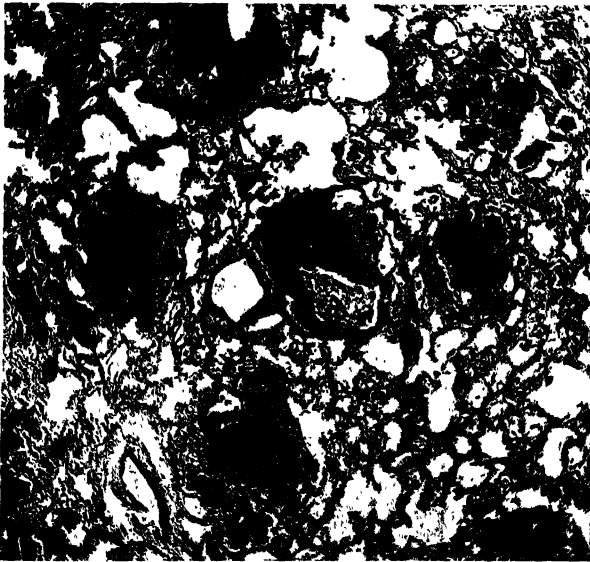
Fig. 320.—*Lung.* Acute Tuberculous Broncho-Pneumonia. ×25.

may shew hæmorrhage, catarrh, or the occurrence of a fibrinous exudate in the air-spaces—a condition resembling acute lobar or lobular pneumonia being produced.

As the condition spreads, little grape-like clusters—the so-called "staphyloid" arrangement—of the tubercle-nodules, which are whitish or yellowish-white in colour, soft, and easily broken down, are seen scattered through the affected area.

Naked-eye Appearances :—

(1) If **the lobular bronchioles** only are affected, minute yellowish nodules are seen, scattered irregularly through the section. They may be slightly raised above the general surface. The nodules may be soft, and sometimes the outline of the bronchiole may be detected in them.

*(2) If the **larger bronchioles** are involved,* the nodules become arranged in groups of from about 2 to 5 mm. in diameter *(see* lower part of fig. 321). These are yellowish in colour, and slightly raised above the surface of the lung. By confluence, larger areas are produced, and the lung presents a mottled appearance, the yellowish tuberculous areas alternating with reddish and congested areas of lung-tissue. The inter-lobular septa may be swollen, and there may be œdema, and fibrinous, or catarrhal, pneumonia in the intervening lung-tissue.

Fig. 321.—*Lung.* Shewing very advanced Acute Caseating Tuberculous Broncho-Pneumonia, with great thickening of the Pleura.

II. CHRONIC TUBERCULOSIS

In this form, the spread is by way of the peribronchial lymphatics, and occurs in the same manner as in the more acute types; but the lesions tend to be larger, and more localised by a growth around them of fibrous tissue, which is often deeply pigmented. They are firmer and larger, have a more definite structure than those of the acute forms, and shew, as a rule, very definite giant-cell systems round the periphery *(see* fig. 322).

Naked-eye Appearances.—Such chronic nodules are characterised especially by : (1) A greater translucency, at any rate in their earlier stage, before the fibrous tissue becomes very dense. (2) Pigmentation, which is due partly to the old accumulation of carbon-pigment at the site of the original peribronchial lymphatics, and also to the increase of pigment which is associated with all chronic irritative conditions. (3) Fibrous overgrowth round the nodule, forming a sort of capsule, either localised or extending into the surrounding lung-tissue, and producing extensive interstitial pneumonia. The centre of the area may shew caseation.

Microscopically, the nodules are composed of fibrous or fibro-cellular tissue, with some caseation in the centre, and generally with definite giant-cell systems at the periphery *(see* fig. 322).

In chronic tuberculosis leading to chronic phthisis, there may be *extensive areas of caseation*, surrounded by proliferated fibrous tissue. These may ulcerate into a bronchus, and thus form **cavities** of various sizes. This invasion of the bronchus may give rise to acute tuberculous bronchitis, and, subsequently, to acute tuberculous broncho-pneumonia. Or again, the nodules may undergo **healing**, *i. e.* become surrounded and shut in by a dense fibrous capsule (fig. 323), the central part usually shewing caseation and sometimes calcification, or the original focus may simply be represented by a dense pigmented and contracted fibrous scar.
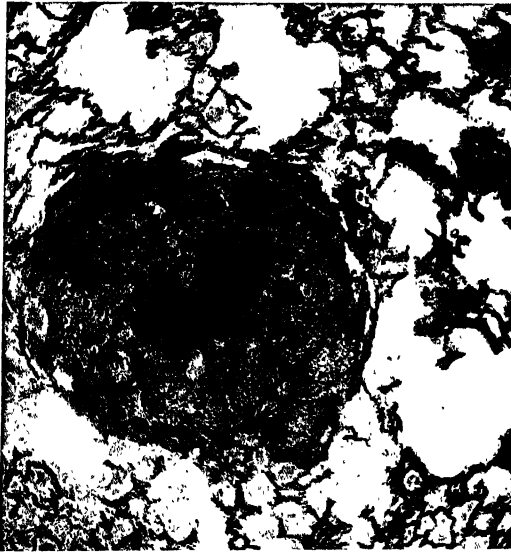
Fig. 322 —*Lung.*   A Nodule in a progressive case of Chronic Tuberculosis, shewing central caseation, giant-cell formation, and peripheral fibrous-tissue overgrowth.   × 50.

FIBROID " HEALED " TUBERCLE :--

In all tuberculous lesions, there may be observed a varying ratio between the processes of destruction produced by the toxins of the bacilli and the processes of reaction against these on the part of the body-tissues. When the latter are successful in localising, or even in entirely neutralising, the effects of the former, they do so to a large extent by proliferation of the connective-tissue elements, which come to surround the diseased area and form a capsule, as it were, which cuts it off from, and prevents its further spread into, the neighbouring tissues. These proliferative changes are, therefore, specially found where the tuberculous process has been arrested, or where its development has been very slow; but they may also develop even in the more acute lesions. Thus, the minute tubercle-granulations of the acute lymphatic type of tuberculosis may shrink, become fibrous, and leave only small scars of pigmented fibrous tissue; or the nodules of broncho-pneumonic

tuberculosis may become surrounded by a zone of fibrous tissue, and the caseous contents of the nodule may dry up and perhaps eventually become calcified. The fibrous overgrowth is especially pronounced in the more chronic peribronchial form. The bronchus—often completely obliterated—and the areas of lung-tissue around it and supplied by it, together with any associated caseous or calcified material, may become surrounded by a zone of dense fibrous tissue, and, at the periphery of this fibrous tissue, a slow extension of the fibrosis into the lung-tissue may be seen (*see* fig. 323). In the later stages, the healing process may be so complete that the tuberculous nature is shewn only by the persistence of giant-cells in the fibrous-tissue nodule.
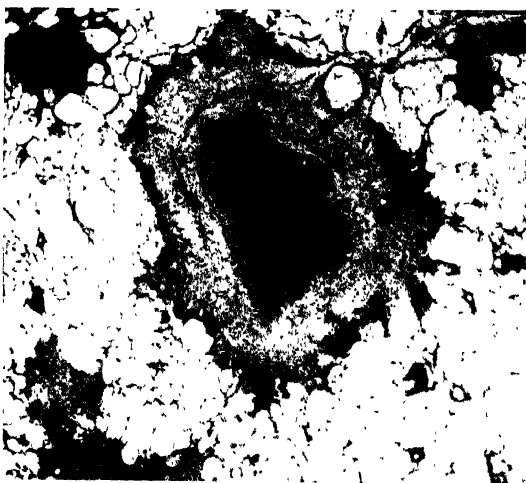
Fig. 323.—*Lung*. Fibroid "Healed" Tubercle. Note the dense fibrous-tissue zone around the central caseous area. × 10.

B.—TUBERCULOSIS WITH CAVITY-FORMATION (PHTHISIS) :

The term "**phthisis**" or "**wasting**" was originally applied *clinically* to the general condition of a patient suffering from certain forms of tuberculosis; and from this it has come to be applied also to the pathological condition of the lung, in which the tuberculous lesion leads to wasting of the lung-tissue with cavity-formation. The pathological processes which are concerned in the production of phthisis are essentially the same as those already described under **Acute** and **Chronic Tuberculosis,** though there is usually a more regular extension of the lesion, combined with greater consolidation of lung-tissue, and always a breaking down and excavation of the caseous tuberculous material, *i. e.* the formation of **cavities.**

The two essential processes in phthisis are **consolidation** and **excavation.** One lung only may be affected, but, very frequently, both are infected from the same source, either simultaneously or at different

periods. The degree of spread is usually *more marked in one lung than in the other, and the characters of the lesions, even in the same lung, often* shew that there have been successive infections.

The disease begins frequently **at or near the root** of the lung, and, from this point, it tends to spread upwards and outwards along the inner aspect of the upper lobe towards the apex, where the condition may be detected clinically. Sometimes, the spread is more directly outwards, and may come to involve the middle part of the upper lobe externally. From the apex, the disease tends at first to spread slowly and continuously downwards by a process of **direct local infiltration**, or by a spread along the pleura; but, at any period, it may suddenly spread **discontinuously,** *i. e.* the infection may be carried to other and more distant parts of the lung. Thus, scattered patches may be found in the lower and posterior parts of the lower lobes, owing to **inhalation** along the bronchi of infected secretion, which gives rise to a **catarrhal or broncho-pneumonic tuberculosis**, often very acute in its progress. In the section of such a lung, there may, therefore, be old chronic tuberculosis or phthisis at the apex, and acute tuberculous broncho-pneumonia in the lower lobe or elsewhere.

The process may also extend along the **peribronchial lymphatics,** until it comes to involve the smallest bronchioles, from which it spreads to the air-vesicles, forming little staphyloid or cluster-like nodules, often shewing marked increase of pigmentation, and giving a granite-like appearance to the section. Overgrowth of fibrous tissue tends to occur around the nodules. Such gradual and progressive fibrous overgrowth is due especially to slow spread along the peribronchial lymphatics. The consolidation extends towards the surface of the lung and gives rise to repeated attacks of pleurisy, which lead to adhesions, and often to considerable fibrous thickening of the pleura over the consolidated areas. Both lungs are usually involved, the disease being generally more advanced in one organ than in the other. The second lung may be infected, either **by way of the bronchial glands and lymphatics,** or **by inhalation** backwards of infected sputum which is being expectorated from the diseased lung.

The pathological appearances which are classified under the term **Phthisis** present many variations. These are due partly to the rate at which changes are produced, partly to the preponderance of one or other type of primary lesion, and partly to the intercurrence of other processes. Thus, the lesions which progress slowly shew a greater degree of fibrous overgrowth, etc., than do those which develop rapidly. Where a broncho-pneumonic form predominates, there is likely to be cavity-formation of a more irregular type than where the prevailing type is lymphatic; and again, a phthisis of slow development may, at any period in its course, assume acute characters and advance rapidly. In addition, there may be changes in the type of the lesion. Thus, a chronic tuberculous peribronchitis may, by the ulceration of the nodule into the bronchus, become

an acute tuberculous broncho-pneumonia, or, by ulceration into a vessel, give rise to the acute miliary form of the disease. Further, the two lungs may shew lesions differing in type.

Thus, it will be seen that, from the consideration of the pathological anatomy or histology of phthisis, it is extremely difficult, or even impossible, in many cases, to draw a definite line of demarcation between the acute and the chronic forms.

It is, however, convenient, for descriptive purposes, to classify the

Fig. 324.—*Lung.* Acute Phthisis, shewing a small cavity with irregular and ragged caseous wall, and also consolidation throughout the remainder of the lung-tissue.   ×35.

condition into cases which are **acute** and those which are **chronic ;** but it must always be remembered that this distinction is one merely of degree and is therefore more or less artificial.

I. ACUTE PHTHISIS :—

Under this term we include only the more rapidly progressing forms of tuberculosis, in which the fundamental lesion is **consolidation** by a tuberculous broncho-pneumonia with necrosis and caseation, followed by **excavation** or **cavity-formation.** The consolidated areas may occur as very minute scattered foci, as larger lobular areas, or as patches

occupying considerable portions of the lung—these larger areas being formed by the confluence of smaller patches. The intervening lung-tissue always shews a varying degree of **congestion** and **œdema,** and very often **acute fibrinous** or **catarrhal pneumonia.** When the tubercles reach the surface of the lung, patches of pleurisy always develop over them. In a certain proportion of cases, the caseous nodule is surrounded by a fibro-cellular zone, in which giant-cells are usually present. This proliferation of fibrous tissue, and the presence of giant-cells, indicate a certain degree of chronicity. The cavities may be rapidly formed and numerous. They are often small and have ragged caseous walls, and may be produced by the **softening and breaking down of caseous broncho-pneumonic areas** or—and probably more frequently—by **ulceration and dilatation of the small bronchi** (*see* fig. 325). In our experience, cavity-formation is comparatively uncommon in young children.

Sometimes, the acute destructive changes and softening may be more extensive and come to involve considerable areas of lung-tissue, producing large cavities, from which the caseated and necrotic tissue may reach the bronchi and be expectorated. The sputum, in such cases, contains fragments of elastic tissue and other elements of the fibrous-tissue framework of the lung, as well as, in some cases, enormous numbers of *B. tuberculosis.*

FIG. 325.—*Lung.* Acute Phthisis, shewing a larger, somewhat chronic cavity at the apex, and also numerous smaller, irregular, acutely-formed cavities in the remainder of the lung-tissue. Many of these cavities are obviously dilated bronchi with ulcerated walls. (Edinburgh University Anatomical Museum. Catalogue No., R. C. f. 6.)

II. CHRONIC PHTHISIS :—

The essential lesion in this form of the disease is **consolidation** brought about by the development of **peribronchial tubercles.** There may, in addition, be nodules in the fibrous tissue of the septa, the deeper layer of the pleura, etc. Around and from these peribronchial areas, proliferation of fibrous tissue takes place and extends into the lung-tissue, producing the condition of **chronic tuberculous interstitial pneumonia,** which may become very extensive, and may be the most obvious lesion.

Cavities are formed by the caseation and softening of the peri-

bronchial nodules and their ulceration into the bronchus, into which the softened material passes and is then expectorated. Perhaps more commonly, the cavities are bronchiectatic in origin. The walls of the bronchus, into which the peribronchial nodule has discharged its contents, become attacked and softened by the spread of the tuberculous process. The bronchi, in this way, are less resistant to the inspiratory efforts, and a gradual, and usually irregular, dilatation takes place, aided, no doubt, by the external traction of the proliferated and contracting fibrous tissue surrounding the affected bronchus. The walls of the bronchi may become completely destroyed, and the bounding layer of the cavity may consist of the proliferated fibrous tissue of the lung- for example, the thickened inter-lobular septa, or even the newly-formed bands of fibrous tissue which are produced by the interstitial pneumonia and which bring about the consolidation in that condition.

Character of the larger cavities.—The chronic cavities are often very irregular in outline, and sometimes sinuous or multi-locular. The lining membrane is smooth and fibrous in the very chronic forms, or coated with caseous material in the less chronic types. The walls of the cavities are often extremely vascular. Crossing the cavities, or projecting from their walls, there are generally bands of fibrous tissue corresponding with the more resistant inter-lobular septa and peribronchial connective tissue, and containing partially obliterated bronchi and vessels. These vessels may become varicose, and, on account of the loss of their support, small aneurisms may form on them, and these may rupture or become eroded by ulceration and give rise to serious hæmorrhage. The cavities, however formed, usually increase in size, not only by progressive ulceration of their walls and distension by long-continued coughing, but by being dragged upon externally by the contracting fibrous tissue of the increasing chronic interstitial pneumonia. The contents of the cavities, composed of caseous and necrotic tissues, may become decomposed owing to the entrance of putrefactive and other bacteria; or pyogenetic bacteria may gain an entrance, giving rise to local suppuration, whilst even septicæmic or pyæmic complications sometimes result from their presence. The infective contents of the cavities, entering the larger bronchi and trachea, may lead to ulceration of these structures, especially marked between the rings of cartilage; and this ulceration may also occur in the larynx. The pleura over the chronic cavities often becomes very much thickened and adherent to the chest wall, this thickening acting as a protection against perforation. Occasionally, however, perforation does occur—usually in the more acute cases—and pyo-pneumothorax may thus result.

Naked-eye Appearances.—In a typical case of chronic phthisis, the pleura of the lung, especially at or over the apex, is much thickened, and dense adhesions to the parietal layer may form. Under this thickened pleura, and usually near the apex, are found cavities, one or more in number, of the character already described. These cavities vary much

in size. They may be small, or, in other cases, a single cavity may occupy the whole of the upper lobe (*see* fig. 326). Throughout the rest of the lung, thickened bands of fibrous tissue are seen, amongst which

FIG. 326.—*Lung.* Chronic Phthisis, shewing a large irregular cavity in the upper lobe. In the lower lobe there are scattered acute nodules grouped in clusters around the small bronchi, and also several small, more acute cavities. The bronchial glands are enlarged and caseous. (Edinburgh University Anatomical Museum. Catalogue No., R. C. g. 10.)

there are, frequently, smaller cavities present, *e. g.* especially in the upper part of the lower lobe; and, in and between the fibrous tissue, whitish or yellowish-white caseous tuberculous nodules may be found, giving rise to

the so-called **fibro-caseous tuberculosis.** *The bronchial glands may shew* small or large areas of caseous transformation.

On microscopical examination, such chronic tuberculous nodules show a caseous centre, with a peripheral fibro-cellular zone, which is often pigmented, either with carbon-particles or with altered blood. Giant-cells are always found in this fibrous tissue; and, associated with these peribronchial nodules, a varying amount of interstitial pneumonia

Fig. 327.—*Lung.* Chronic Phthisis. This section is taken from a part in which cavity-formation is almost absent. It shews the irregular tuberculous nodules (with caseous centre, giant-cells, and fibro-cellular zone) which have fused to form dense consolidated areas. Note the "pseudo-glandular" character which the alveolar spaces have assumed (*cf.* Interstitial Pneumonia). ×35.

occurs at places, often giving rise to dense masses of consolidation in which groups of caseous tubercle-nodules are seen (fig. 327).

The **bronchial glands** may shew minute foci of tuberculosis, with giant-cell systems, or caseation throughout. **Calcification** is very common; and **waxy** or **amyloid degeneration** may also, in some instances, especially in very chronic cases, be demonstrable in them.

HÆMORRHAGE FROM PHTHISICAL LUNGS :—

Hæmorrhage may occur at various periods of the disease. In early cases it may be due to—

(i) The softening and ulceration of a peribronchial tuberculous nodule, forming a communication between a bronchus and a branch of the pulmonary artery (or possibly a tributary of the vein) *or a bronchial vessel.* This is probably one of the most important causes of **early hæmoptysis.**

(ii) The **ulceration of the wall of a cavity opening into a small vessel.** As the effused blood often contains *B. tuberculosis,* and is inhaled into other bronchi, these hæmorrhages may give rise to an acute spread of the disease, the blood acting as a " culture-medium," as it were, for the growth of the bacillus, and also assisting its attack by acting as an irritating foreign body. It is also possible that some of the bacilli may get into the blood in the pulmonary artery, and so cause an acute blood-spread.

Later in the course of the disease, hæmorrhage may be caused by—

(i) The **ulceration of the walls of a cavity eroding and opening into blood-vessels.**

(ii) The **engorgement and rupture of capillaries** in the vascular walls of cavities, giving rise to a condition of oozing from the walls.

(iii) **Rupture of, or erosion into, small aneurisms** on branches of the pulmonary artery. Such rupture, of even a very minute aneurism in the walls of a cavity or in some of the fibrous bands traversing it, may lead to a fatal hæmorrhage.

(iv) **Ulceration into a tributary of the pulmonary vein** is not common, but may occur.

(v) **Rapid softening and breaking down of a large area of lung-tissue** may cause hæmorrhage by **opening into the vessels.** Except in extremely acute cases, such a result is not frequent, because the vessels round the tuberculous focus usually undergo obliteration—the tuberculous area itself being thus non-vascular.

TUMOURS OF THE LUNG :—

PRIMARY TUMOURS are extremely rare. **Osteomas, chondromas,** and **sarcomas,** occur, but the most usual primary tumours are **columnar-celled cancers**—originating, probably, from some part of the bronchi or from the mucous glands—and **mesotheliomas (endotheliomas)** arising from the endothelium of the lymphatics of the deeper layer of the pleura.

SECONDARY TUMOURS are frequently seen in the lung. All forms of **sarcoma** and of **cancer** may occur. Direct spread of lympho-sarcomas of the mediastinal glands into the lung-tissue is common. The secondary growths of certain **tumours of bone,** especially **sarcomas**—because of their tendency to spread by the blood-vessels—and of **chorion-epithelioma,** have their seat of election in the lungs.

PARASITES :—

Hydatids are not infrequent, and are found especially in the right

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blower loe. Of the others, the most important are certain **lung-flukes** (*Paragonimus ringeri, P. westermani*, and *P. kellicotti*) the ova of which are found in the sputum (*see* p. 390). In **filariasis,** the *Microfilariæ* are found congregated in the blood-vessels of the lung during the periods in which they are absent from the peripheral blood. *Filaria bronchialis* is unusual in man. Abscesses caused by *Entamœba histolytica*, and secondary to dysenteric ulceration of the intestine or to amœbic abscess of the liver, are occasionally found. These conditions are discussed in the section on **Animal Parasites,** as is also the migration of *Ankylostoma*, *via* the lungs and bronchi, on its way from the skin-surface to its habitat, the upper part of the small intestine.

' DISEASES OF THE PLEURA

HYDROTHORAX.—Normally, the pleural cavity contains a very slight amount of fluid; but there may be an increase in its amount during the hours before death. Thus, a small amount of fluid found in the pleural cavities at a *post-mortem* examination may be of little pathological significance. Larger accumulations, however, may occur as part of a general dropsy in cardiac or in renal disease, and to this condition the term **Hydrothorax** is applied. They are usually bilateral, though the amount of fluid may be larger in one pleural cavity than in the other; but a unilateral condition may occur, as, for example, from pressure on the veins of one side by tumours, or without obvious cause, as in Bright's disease, in which this unilateral hydrothorax is sometimes present. The fluid presents the ordinary characters of a serous transudate. The pleura itself may become diffusely thickened and opaque, or even œdematous, as a result of the collection of fluid, and the lungs may become extensively collapsed. If adhesions are present, these, and also the lung-tissue, may become œdematous, and no fluid may be found in the pleural sac.

HÆMORRHAGE.—Small sub-pleural ecchymoses are seen in various forms of infective diseases (*e. g.* the acute fevers and septicæmias), in blood-diseases such as pernicious anæmia, in purpura, in cases of asphyxia, and in some cases of chronic venous congestion.

Larger Hæmorrhages, constituting the condition of **Hæmothorax,** may be due to wounds of the chest-wall or lung causing laceration of blood-vessels, to fracture of the ribs, to rupture of aneurisms into the pleural sac, or to the presence of tumours. **Hæmothorax** is a frequent complication of war-wounds of the chest. The fluid consists, in the main, of defibrinated blood, which does not undergo massive clotting when removed from the chest. The lung is very frequently collapsed, especially the lower lobe. The portion of the lung above the fluid may shew very marked emphysema.

Very often, at the upper limit of the effused blood, are found loose fibrinous adhesions glueing the surface of the lung to the chest-wall;

whereas, in the area of effused blood, both the parietal pleura and the collapsed lung become coated with a thick layer of fibrin. The collapsed lung, especially if it is not lacerated, very rarely shews any evidence of pneumonia or even acute hyperæmia. Infection does not necessarily take place, but may occur early or late in the process. In the infected cases, the exudate contains many inflammatory cells (polymorphonuclear leucocytes, etc.), the fibrin-deposit on the pleura is more marked, and there may be a considerable development of gas from the gas-producing anaerobes. This gas has an offensive smell, often accumulates under considerable pressure, and may be collected above the septic blood, isolated by adhesions, or may occur at isolated points in the midst of an infected hæmothorax. Henry found that such organisms as *Pneumococci, B. influenzæ* and *M. tetragenus* were found in twenty per cent. of his cases, and that, in the remaining eighty per cent., the principal organisms were *Streptococci, Staphylococci,* and anaerobic gas-forming bacilli, and, in approximately fifty per cent. of his infected cases, anaerobic bacilli, either alone or in association with cocci, were found.

In **aseptic hæmothorax,** the fibrin which is found on the pleura is probably precipitated fibrin resulting from the defibrination brought about by the cardiac and respiratory movements.

In **septic hæmothorax,** in addition to the fibrin seen in the aseptic cases, there is a secondary inflammatory deposit of fibrin from the pleural effusion. This may be very slight, or a thick, ragged, shaggy spongework, containing gelatinous pus in its interstices.

The **source of the blood,** in these cases of hæmothorax resulting from gunshot wounds, may be the vessels in the chest-wall, but, after careful observation, Henry and Elliott conclude that, in the majority of their cases, the hæmorrhage came from the lacerated vessels in the lung.

PNEUMOTHORAX.—The accumulation of air or gas in the pleural cavity, for which this term is used, may be either **general,** or **localised by adhesions.** It may be due to the entrance of air, either from without, or from the lung. A wound of the chest-wall or a wound of the lung may thus give rise to it, or it may be caused by rupture or ulceration of the lung-tissue. The ulceration may result from the softening and breaking down of a septic infarct, or be produced in a minute bronchiectatic or tuberculous cavity which is in direct communication with a bronchus; and, in either case, it may produce a communication between the air-tissue of the lung and the pleural cavity. Rupture of the lung-tissue may occur during excessive exertion—for example, during the paroxysms of whooping-cough or a severe attack of coughing, especially if the lung is emphysematous.

The condition is also, but much less commonly, produced by the ulceration of a suppurating or tuberculous bronchial gland into a bronchus and also into the pleural cavity; or by the perforation into the pleural cavity of an ulcer of the stomach which has become adherent

to the diaphragm. It may be caused by the gas formed by the organisms *during life. These are usually anaerobes.* Henry and Elliott[1] found that *this was the general type of* **pneumothorax** *resulting from wounds of the thorax,* and that the presence of air derived from the lung itself was very uncommon. No doubt some air must escape through the damaged lung-tissue, but, apparently, this is small in amount and is soon absorbed.

Results.—The most important complications or sequelæ of this condition are collapse of the lungs, and, especially if septic organisms are introduced, inflammation, suppuration, hæmorrhage, etc., and the production of pyo- and hæmo-pneumothorax.

ACUTE INFLAMMATION (PLEURISY or PLEURITIS) may result from local or from general causes. Among the **local causes,** the most important is extension of the inflammatory process from adjacent parts— for example, from the lungs in cases of pneumonia, septic infarction, gangrene, or tuberculosis: from the heart in pericarditis: from acute inflammatory conditions of the mediastinum, of the ribs, or of the chest-wall: from the abdomen, by way of the lymphatics of the diaphragm, in peritonitis or in other abdominal affections; or it may be due to traumatism of the chest-wall or of the lung. In the group of **general** causes, those conditions which involve the pleuræ by way of the circulating blood may be mentioned. In the main, the irritants are of bacterial or toxic origin, though the nature of some is obscure or entirely unknown. Cases of pleurisy which occur in **pyæmia** and **septicæmia, acute rheumatism** and other **acute infective diseases,** and in **tuberculosis,** are, no doubt, due to the direct action of bacteria or of the poisons produced by them. A possible cause of the pleurisy which occurs in some cases of **Bright's disease** and **scurvy** is the presence of some metabolic poison which may act in a similar way to the toxins of bacteria; but, in the majority of such cases, these poisons—if present—merely predispose the tissues to organismal infection. Certain forms of pleurisy are secondary to **tuberculosis** or **cancer** of the pleura. When, however, all these causes have been excluded, there still remains a small residuum of cases in which the origin of the condition is uncertain. These, until their cause has been ascertained, are classed as cases of **idiopathic** pleurisy. Some of these are undoubtedly **tuberculous** in origin, and, if a systematic and thorough examination were made by inoculation into guinea-pigs, we feel sure that the number of so-called idiopathic cases would be very small.

Morbid Anatomy.—Several forms of acute pleurisy may be distinguished, though one form, at a later period, often passes into another. Of these, the most important are the **dry** or **fibrinous, the serous** or **sero-fibrinous,** the **purulent,** and the **hæmorrhagic.** An acute attack is often superimposed on a chronic one, and fibrin may be deposited on the thickened and adherent pleura. Thus, a new attack of acute pleurisy may occur in portions of pleura still unobliterated by adhesions due to

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[1] Herbert Henry and T. R. Elliott, " The Morbid Anatomy of Wounds of the ax," *Jour. R.A.M.C.,* vol. xxvii., 1916, p. 525.

a previous pleurisy which may have been caused by the same, or by some other, variety of organism.

(a) **Dry or Fibrinous Pleurisy.**—*This begins with the usual inflammatory phenomena of dilatation of vessels, exudation of lymph, and emigration of leucocytes.* The lymph becomes coagulated, and is deposited in the form of fibrin on the pleural surface. This lymph, at first a thin white or greyish pellicle, soon becomes yellowish, and increases considerably in thickness. The process may be confined to small localised areas of the pleura, or may be very widely spread. The **microscopical**

Fig. 328.—*Acute Pleurisy.* Shewing a deposit of fibrin and leucocytes on the surface of the pleura. × 60.

appearances are in no way different from those of an ordinary inflammatory exudate on any serous surface. The deposit generally takes place on both the visceral and the costal pleura; and adhesions between these two surfaces, or between the adjacent layers of visceral pleura lining the inter-lobar sulci, are thus formed. The exudate may, at a later period, be absorbed; or definite organisation and the formation of connective tissue, diffusely or in bands, be produced. If adhesions do not take place, the organisation leads to chronic thickening of the pleura. The organisms concerned in this process are probably mainly *Streptococci* (e. g. *S. rheumaticus*) and the *Pneumococcus*.

. *(b)* **Serous or Sero-Fibrinous Pleurisy.**—This may be a further stage of the fibrinous variety; but, frequently, the serous exudation occurs early in the inflammatory process, and develops very rapidly. The amount of fluid is determined, to some extent, by the presence or absence of adhesions in the pleural sac; and, if there are no adhesions, the sac may be almost completely filled with fluid, the lung being pressed backwards and inwards towards its root, and becoming practically completely collapsed; and the heart and pericardium displaced towards the middle line or to the opposite side of the chest. The pleura itself shews a more or less extensive coating of fibrinous exudate.

Characters of the Fluid.—The serous exudate, if rapidly formed, closely resembles dropsical fluid, but, usually, it contains more albuminous material. Leucocytes may be scanty or very numerous. Their characters vary with the nature of the causal condition and the acuteness of the process. Thus, in the pleural inflammations caused by pyogenetic organisms, e. g. *Pneumococci, Staphylococci,* or *Streptococci,* the **polymorphonuclear leucocytes** predominate in the early stages; whereas, in those caused by *B. tuberculosis,* the **lymphocytes,** or cells indistinguishable from these, are the principal cells present. Again, in more chronic inflammatory cases, the proportion of mononucleated cells of various kinds is considerably increased.

Results of the Process.—The fluid may become absorbed, and the epithelium be restored to its normal condition. More frequently, however, adhesions are formed,·at first delicate and somewhat cellular, but, later, composed of dense fibrous tissue, by which the lung and chest-wall become closely bound in apposition to one another. In certain cases, fibrous bands of considerable length pass between the lung and the chest-wall.

(c) **Purulent Pleurisy (Empyema).**—This condition is sometimes secondary to other forms of pleurisy, but, more commonly, it is a suppurative affection from the beginning. It is very difficult and, in many cases, impossible, to draw a clear distinction between pleurisy and empyema. Both are inflammatory processes caused by bacteria, and, whether the condition is suppurative or what is called non-suppurative, depends on various factors, e. g. duration, character of organisms, etc.

Ætiology.—The suppurative process may spread **directly** from the lung in cases of acute lobar pneumonia, septic pneumonia, septic infarction, bronchiectasis, abscess of the lung, or tuberculosis, especially where a cavity has perforated; it may be **secondary** to diseases of the chest-wall, e. g. ribs, and occasionally the vertebræ: or to peritonitis or to any suppurative condition below the diaphragm in connection with the liver, spleen, stomach, or intestines; or it may arise in the course of pyæmia, the infective agent being carried to the pleura by the blood-stream. Of the organisms found, either alone or in association with one another, the commonest are the *Pneumococcus* and the *Streptococcus pyogenes;*

Staphylococci and *B. pneumoniœ* are not infrequently found, and *B. tuberculosis* is sometimes the causal organism, especially in cases arising from the rupture of a tuberculous focus in the lung or elsewhere. In individual cases, *B. coli communis, M. tetragenus, Streptothrix actinomyces,* various forms of *Leptothrix,* etc., have each been described as the only organisms present, and, therefore, possibly causal of the condition. In certain cases, the purulent fluid has a very foul odour, and, in ˉthese so-called " **putrid empyemas**," various large, and at present unclassified, bacilli have been demonstrated. In such cases, gas is often present.

Sites.—The collection of pus is found at any part of the pleural cavity, but its commonest situation is over the lower and outer aspect of the lower lobe. If there are no adhesions, the spread becomes general, and an enormous quantity of pus—usually pale greenish- or yellowish-white in colour, varying in consistence, and perhaps containing shreds of coagulated lymph--collects. The purulent exudate is sometimes confined to the surface of the diaphragm or to an interlobar sulcus.

Results.—These may be classified as follows :—

1. **Collapse of the lung** takes place to a varying degree, depending on the amount of fluid, and on the extent of the adhesions, if present.

2. **The pus sometimes burrows**, especially along the lines of the intercostal spaces, and accumulates in the subcutaneous tissues of the thorax: or it may make its way downwards between the pillars of the diaphragm, and form an abscess round the kidney, or it may even reach and come to the surface in the inguinal or gluteal regions.

3. **Perforation into the lung** and partial evacuation of the contents through the bronchi may take place, giving rise to purulent expectoration, with inflammation in both the bronchi and the tissue of the lung. Air sometimes enters the pleural cavity by this new channel, and gives rise to **pyo-pneumothorax ;** and, if putrefactive bacteria gain admission, the pus assumes a very putrid character.

4. The fluid part of the pus may undergo absorption, leaving **inspissated caseous material** which becomes **calcified,** and—the pleura becoming greatly thickened—re-expansion of the collapsed lung, which has become extensively fibrous, is prevented. The chest-wall is dragged in, and the pericardium and heart, as well as the opposite lung, may be pulled across the middle line.

(*d*) **Hæmorrhagic Pleurisy.**—The only special character presented by this variety is that the fluid contains a considerable amount of blood, and, in some cases, the exudate is composed of this almost entirely. The condition is associated especially with **tuberculous** and **malignant** diseases of the lungs and pleura. In cases of malignant disease, tumour-cells are sometimes recognised in the fluid; but, unless they occur in distinct clumps and masses, it is often extremely difficult, or even
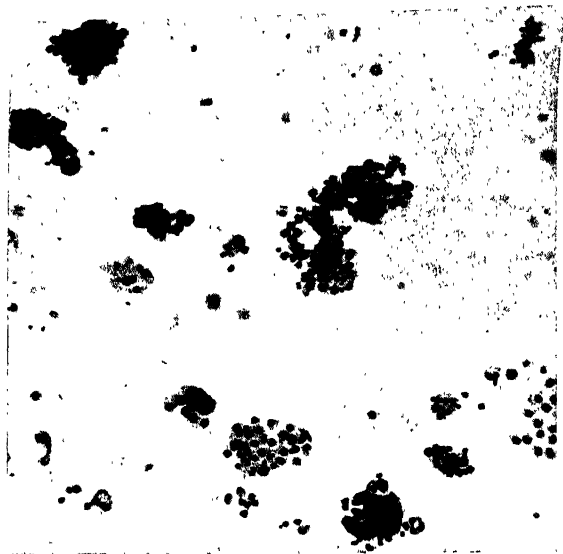
Fig. 329.—*Mesothelioma* (" *Endothelioma* ") *of Lung.* Masses of tumour-cells in pleural fluid. × 75.
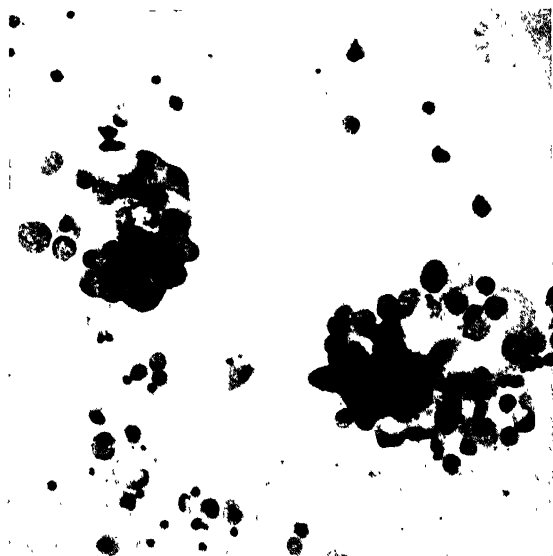
Fig. 330.—*Mesothelioma* (" *Endothelioma* ") *of Lung.* Masses of tumour-cells in pleural fluid. × 300.

impossible, to distinguish them from some of the mononucleated cells which are present in the exudate in cases of pleurisy. Hæmorrhagic *effusion may occur also in the pleurisy, sometimes found in Bright's disease, in certain blood-diseases, in scurvy, or similar conditions.*

CHRONIC PLEURISY.—This term is generally applied to a fibrous thickening of the visceral layer of the pleura, the result of repeated acute attacks, or of that proliferative and protective process, which is found especially in cases of chronic phthisis.

• **Localised chronic fibrous thickenings of the pleura** have been referred to under the various forms of chronic interstitial pneumonia. They are common in elderly people, and occur specially at the points where the
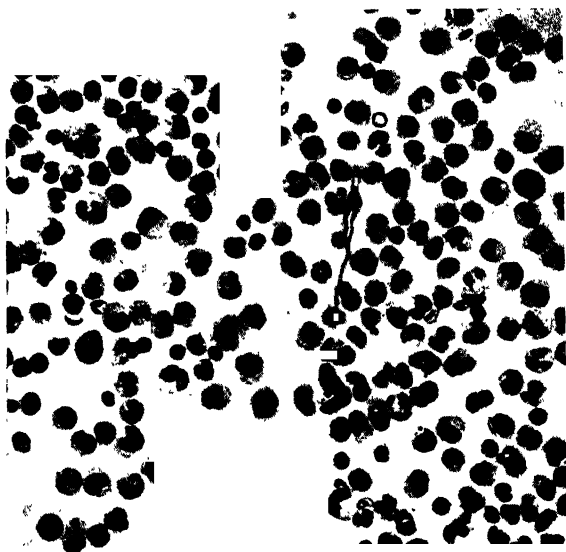
Fig. 331.—*Pleural Fluid* (film of centrifugalised deposit), from a case of lymphosarcoma of mediastinal glands invading lung and pleura. × 300.

inter-lobular septa meet the deep layer of the pleura. They may be formed around accumulations of pigment, or of other foreign material such as stone-particles, etc., or—if not, as they frequently are, of chronic tuberculous nature—are probably due to obliterative changes in small vessels.

TUBERCULOSIS OF THE PLEURA :—

This condition is either **primary** or **secondary.** The former is said to be rare, but, according to the work of Washbourn, the condition is much commoner than is generally supposed. In these primary cases, the appearances resemble very closely those seen in acute non-tuberculous
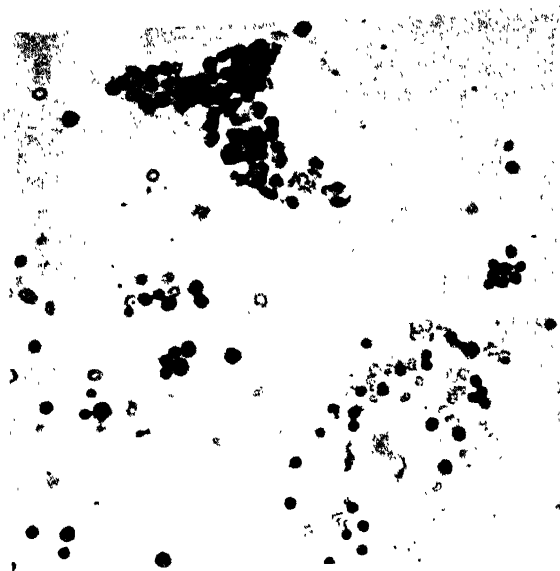
Fig. 332.—*Pleural Fluid*, shewing lympho-sarcoma cells and red blood-corpuscles, from a case of lympho-sarcoma of the lung.   × 300.

Fig. 333.—*Pleural Fluid*, from a case of cancer of the lung. Section of fibrinous clot shewing little entangled clumps of tumour-cells.   × 100.

pleurisy. The exudate, however, is usually rich in lymphocytes, and the presence of *B. tuberculosis*, where microscopical examination fails to demonstrate it, may be detected by inoculation-experiments. It is not uncommon, especially in children, to find *Strepto-* and *Pneumo-cocci* in addition to *B. tuberculosis*, in which case the exudate may contain polymorphonuclear leucocytes in great abundance.

The secondary forms have been described under **Tuberculosis of the Lungs.**

· TUMOURS :—

Primary Tumours are rare. **Fibromas, lipomas, chondromas, osteomas, sarcomas** (especially the spindle-celled variety), and **cancer,** have been described. **Primary mesotheliomas (endotheliomas),** starting in the lymphatics of the deep layer of the pleura, occur.

Secondary Growths of **sarcomas** and **carcinomas** are of more frequent occurrence.

PARASITES :—

Echinococcus cysts (Hydatids) are the only important parasites found in the pleural cavity.

DISEASES OF THE DIGESTIVE SYSTEM

DISEASES OF THE MOUTH

MALFORMATIONS:—

Various **clefts** and **fissures** have been described in connection with the lower lip, the palate and nasal bones, etc., but the most frequent developmental defects, in this region, are **cleft-palate** and **hare-lip**. To understand these abnormalities, it is necessary to remember that, in the development of the primitive palate, there are three parts concerned : (1) a **premaxillary**

Fig. 334.—Single Hare-lip with cleft-palate.   (From a case of Sir Harold Stiles.)

and **vomerine** part developed between the nasal passages, and (2) a **right** and (3) **left maxillary part,** laid down on the outer aspect of each passage; and, further, that, in the formation of the face, five processes, which begin to spring from the base of the primitive cerebral capsule towards the end of the third week of fœtal life, have to be considered.   These five are illustrated in fig. 335, and the two, which are of special importance in the formation of the lips and palate are the **nasal,** composed of symmetrical right and left halves, and the **maxillary, processes.**

The **mesial nasal process** forms the whole septum of the nose, the premaxillary part of the upper jaw and the middle third of the upper lip.

The **maxillary process,** in front, comes in contact and fuses with that part of the mesial nasal process which forms the **premaxillary** part of the

Premaxilla
(Mesial Nasal
Process)

Upper Lip
(Mesial Nasal Process)

Upper Lip
(Maxillary Process)

Maxillary Process
(Palate spreading in
the Line of Arrow)

Dotted Line along any part of which
union may fail

Mid Brain

Cerebral
Vesicle

Mesial
Nasal Process

Lateral Nasal
Process

Maxillary
Process

FIG. 335

Maxillary
Process

Mesial
Nasal Process
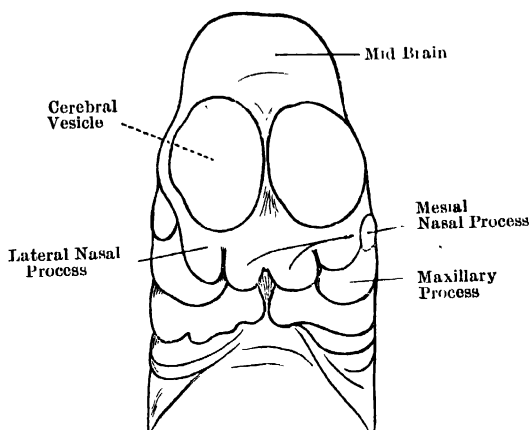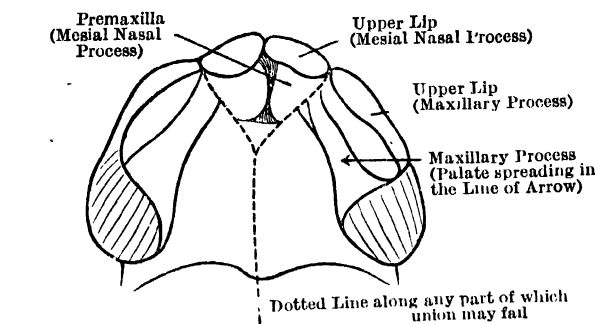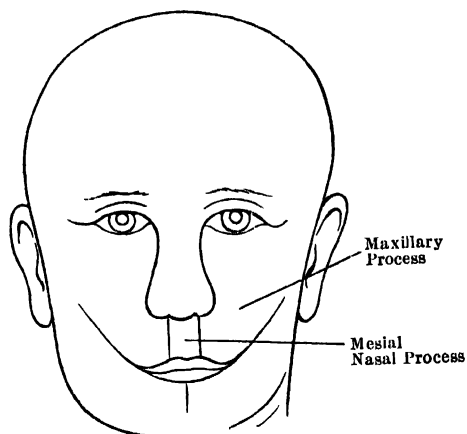
FIG. 336.

upper jaw and the middle part of the upper lip. The **hard palate** (with the exception of the premaxillary part) is formed by a horizontal plate which grows inwards from the maxillary process on each side and fuses with the plate of the opposite side. The lines of union are indicated in fig. 335.

In **hare-lip,** there is a failure of union between the mesial nasal process which forms the middle third of the upper lip and the maxillary process which form the lateral parts. This failure of union may be unilateral or bilateral, producing single or double hare-lip respectively, or it may occur only to a limited degree on one side, and may be represented by a mere notch on the margin of the lip.

In **cleft palate,** all degrees of non-union are found—from a slight

FIG. 337—Double Hare-lip, shewing the premaxillary mass, etc., front view.

FIG. 338.—Side-view of same shewing projecting premaxillary mass.

(From a case of Sir Harold Stiles.)

splitting of the uvula posteriorly to complete fissure of the palate, with cleft of the lip on each side. The cleft in the palate will necessarily always be single and mesial behind the premaxillary bone, but anteriorly it may run on one or both sides of the premaxilla.

A condition of median hare-lip in man has been described, but it is so rare that it is not necessary for us to discuss its method of formation.

Under the terms **Macroglossia** and **Macrocheilia,** congenital enlargements of the tongue and of the lips respectively are usually described. **Macroglossia,** or enlargement of the tongue, may occur in **Acromegaly,** the enlargement being due partly to the thickening of the mucous membrane, and partly to the increase of the inter-muscular cellular tissue. **Lymphangiomatous enlargement,** due to distension of the lymphatic spaces, with subsequent thickening and induration of the lingual tissue, is perhaps the most usual form of macroglossia. **Muscular enlargement,**

due to an increase in the number and size of the muscular fibres, has been described in cretins and congenital idiots.

In **Lymphatism,** the papillæ and lymphoid tissue at the root of the tongue are often considerably hypertrophied, a point of some importance in the diagnosis of the condition during life.

Abnormal fixation of the tongue—**Ankyloglossia**—may be due to imperfect development of the tongue or to a short and adherent frænum.

DEGENERATIONS :—

Waxy or **amyloid** degeneration has been described as occurring in the tongue, and **fatty** changes are seen in wasting diseases; but both conditions are unimportant. In **myxœdema,** the degenerative changes are usually well marked in the tongue.

ATROPHY of the tongue may occur in association with degenerative changes in the nucleus of the hypoglossal nerve, as in bulbar paralysis.

INFLAMMATION :—

Inflammation of the mucous membrane of the mouth **(stomatitis)** may occur in varying degrees.

(a) **CATARRH.**—This condition occurs in acute fevers, e.g. typhus, typhoid, and scarlet fevers, etc., and it also arises from the irritation of carious teeth and similar causes. The mucous membrane becomes red and swollen, and there is a great increase in the desquamation of the surface epithelium, and also in lymph-transudation and leucocyte-emigration. The desquamated epithelium becomes mixed with the exuded fluid and the leucocytes, and a thick layer may gather, especially upon the tongue—"**Furred tongue.**" In this "fur," various bacteria, mostly normal inhabitants of the mouth, are found in large numbers.[1] Frequently, the inflammatory process specially affects the mucous glands, so that prominent nodules or even vesicles are formed. This condition of **follicular stomatitis** may lead, by rupture of the vesicles, to **follicular ulceration.**

(b) **APHTHOUS STOMATITIS** (Thrush) occurs principally in young and unhealthy children, but may also attack weakened adults. The condition is due to the presence of a fungus—*Oïdium albicans* or *Saccharomyces albicans*—and is distinguished by the presence on the mucous membrane, especially of the lower lips and gums, of irregular, opaque, whitish areas. These patches are more or less adherent, and are composed of masses of desquamated epithelium united by branching threads, consisting of the elongated cells and spores of the fungus.

(c) **GANGRENOUS STOMATITIS** (Noma or Cancrum oris) affects the mucous membrane of the cheeks in badly-nourished children, especially

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[1] An extraordinary degree of **hyperplasia of the filiform lingual papillæ** (up to half-an-inch in length) has been observed by Carnegie Dickson, in a case of **mycosis** of the tongue, the organism associated with the condition being *Rhizopus niger.* The glossitis, in this case, was characterised by marked hyperkeratosis of the papillary filaments, and by blackish pigmentation—**Melanoglossia.**

in those recovering from some severe illness, such as measles or scarlet fever. At first, there is seen on the outer surface of the cheek a diffuse swelling—firm and red, with, as a rule, a darker centre. The inner side of the cheek shews an intense inflammatory reaction, with, usually, a central irregular ulcer, at the base of which there is a dark sloughing mass. The condition spreads extremely rapidly, with extension to, and necrosis of, all the tissues of the cheeks and lips. It commonly involves the gums also, and even necrosis of the jaw may result. The advancing edge is always intensely red, and shews all the usual phenomena of inflammatory reaction in a very marked degree. Pseudo-diphtheria bacilli, *B. fusi-formis*, various spirochætes, Leptothrix-like organisms, streptobacilli, and other bacteria, have been found in the necrosed and necrosing tissue; but the specific pathogenetic relationship of any one of these to the disease has not been established.

(*d*) **Other forms of STOMATITIS** may occur, giving rise to necrotic and ulcerative changes. In **smallpox,** the vesicles which form in the mouth may rupture and give rise to ulcers. In **scurvy,** the spongy swelling of the gums may result in ulceration round, and loosening of, the teeth, or even in necrosis of the bones of the jaw. In the severe form of stomatitis due to the prolonged absorption of **mercury,** there is always associated pyorrhœa, the mucous membrane of the gums and cheeks becomes very much swollen, the teeth may become loosened and drop out, and ulceration of the gums frequently follows.

INFLAMMATION OF THE TONGUE OR GLOSSITIS (*see also under* **Catarrh,** p. 735), most commonly occurs as a result of injury from without; but it may be produced by the irritation of carious teeth, or by the extension of a neighbouring erysipelatous area. The whole organ becomes swollen, and the tissues are infiltrated with inflammatory products, but suppuration very rarely occurs. The condition sometimes persists and assumes a chronic form, bluish-white, pearly patches—which may be smooth or warty, and which are due to a hyperplasia of the epithelium, with usually some evidence of chronic inflammatory change in the deeper tissues—appearing on the tongue. To this condition, various names, such as Leucoplakia, Keratosis, Psoriasis, Tylosis, Ichthyosis, etc., have been given. According to Hunter, glossitis is a common precursor of pernicious anæmia.

GRANULOMATA :—

(*a*) **SYPHILIS** presents itself in various forms in the mouth. The lesions are frequently **secondary,** but the **primary chancre** may occur in this situation, especially on the lips. Of the secondary lesions, the commonest are the **mucous patches, flat condylomata,** or **warts,** which frequently break down to form superficial ulcers. **Gummata,** if deeply situated, may give rise to extensive necrosis and ulceration, with considerable loss of substance of the tongue and neighbouring parts. The

healing of these deep ulcers gives rise to large areas of cicatrisation, which may lead to deformity of the tongue.

(*b*) **TUBERCULOSIS** is comparatively uncommon in the mouth, and is usually secondary to affections of the pharynx or larynx, or to pulmonary tuberculosis. The ulceration, which sometimes simulates very closely epithelioma, usually occurs on the dorsum or at the margins of the tongue; but tuberculous nodules may also be found at its root. Small nodular masses are formed, which undergo caseation, and in some cases ulceration. " **Tuberculous papillomata** " have been described, but these are usually masses of granulation tissue formed in connection with fissures of the tongue, and subsequently infected with *B. tuberculosis.* **Lupus** of the face may spread so as to involve the mouth.

(*c*) **LEPROSY.**—Nodular masses of granulation-tissue, similar to those found in the skin, occur in the mucous membranes of the mouth and tongue.

(*d*) **ACTINOMYCOSIS** and other mycotic infections may invade the tongue (*see* p. 240, *General Pathology ;* and note on p. 735).

TUMOURS AND CYSTS :—

Simple tumours, such as **fibromas, lipomas, myxomas, chondromas,** and **papillomas,** occur in the submucous tissue of the mouth or tongue. **Angiomas,** composed both of blood-vessels (Hæmangiomas) and of lymphatic vessels (Lymphangiomas), are found on the tongue and lips.

Fig. 339.—*Squamous Epithelioma of Lip.* Shewing ulceration of the irregular warty-looking tumour, with raised indurated edges. (Edinburgh University Anatomical Museum. Catalogue No., T. C. a. 6.)

Sarcomas are rare, unless they have extended from other parts, *e. g.* a myeloid sarcoma, growing from the jaw, may form a projecting mass in the mouth. **Carcinomas** are the most important tumours of the mouth. They are very common, and are generally epitheliomas of squamous-celled type, their most frequent sites being the lower lip and the tongue (*see* fig. 339).

Cystic formation, due to the blocking of the ducts of mucous glands, occurs upon the tongue and the lips, and one form (**Ranula**), due to

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closure and distension of the duct of a mucous gland, or of the submaxillary or sublingual glands, occurs beneath the tongue (*see* pp. 344 and 744). Dermoid cysts due to developmental irregularities in the obliteration of branchial clefts, etc., may occur.

DISEASES OF THE TEETH

Only the very briefest reference need here be made to some of the commoner affections of the teeth.

1. **Caries** of the teeth consists in the gradual solution of the lime-salts, with softening and disintegration of the enamel and the dentine, and the formation of a somewhat granular, brown or brownish-black detritus. In this degenerated material, numerous spirochætes, *Leptothrix* filaments and other bacteria are found, and are considered by some authorities as causal. The bacteria probably act by producing acids, which attack thinned or fissured portions of the enamel. The destructive processes may penetrate to the pulp of the teeth, and there set up inflammation and suppuration, producing, secondarily, alveolar abscesses (gumboils), or even necrosis of the jaw. Inflammation, suppuration, and abscess-formation in the gums, may occur independently of dental caries.

2. **Congenital Syphilis** gives rise to the characteristic " Hutchinson's teeth." The upper central incisors are narrow and pointed (peg-shaped), the cutting edge being smaller than the base of the crown, and having on it a well-marked crescentic notch.

3. **Tumours and Cysts.**—The cement-substance occasionally shews a hypertrophic condition, sometimes described as an **exostosis** or **osteoma**. It is really the result of chronic inflammatory changes, and not a true tumour. **Odontoma** is the name given to a tumour which arises, as a result of mal-development, from teeth retained in the alveoli. It is composed of dentine and enamel.

Dentigerous Cysts are produced by dilatation of the dental follicles. These sometimes reach a large size.

DISEASES OF THE JAW

INFLAMMATION :—

Diffuse periostitis may follow an injury, the irritation of a dental plate, sepsis or caries of the teeth, prolonged exposure to the fumes of yellow phosphorus, or the administration of mercury, and it is sometimes a sequel of some of the acute infective diseases. More commonly, however, the inflammatory condition is localised, forming an acute **alveolar abscess** or a more chronic condition, such as **pyorrhœa alveolaris.** In the former condition, the infective agent generally gains entrance through a carious area in a tooth, and, spreading to the pulp, infects the deeper parts of the socket. The cement may become detached from the periosteum, the pus raising up the tissues and forming an abscess outside the bone, and, eventually, passing out through the gum on a level with the apex of the affected fang or between the gum and the neck of the tooth. More rarely, the opening is into the antrum, or externally, through the cheek. **Pyorrhœa alveolaris** is usually at first confined to one or two

teeth, especially the lower incisors. It is also seen round "crowned" teeth. Later, unless treated, it tends to spread until all the teeth have become involved. There is usually marked congestion of the gums and some hæmorrhage. With ulceration and destruction of the periodontal membrane, the alveolar margin is gradually absorbed, and pockets are left between the teeth and the swollen gum, pus collects in these areas and eventually the teeth may be exposed from crown to fang, and, if untreated, they gradually drop out. Various authors have attributed such diseases of the joints as osteo-arthritis, rheumatoid arthritis, etc., to the absorption of poisons from septic conditions of the gums and jaw, and, in the pyorrhœa associated with these rheumatic affections, a varying admixture of *Streptococci, Streptobacilli, B. fusiformis, Spirochœtes, Leptothrix,* and other filamentous organisms, and other bacilli and cocci is usually present. In many cases, streptococci are the predominating organisms and their association with rheumatic affections is worthy of note.

Inflammatory and necrotic changes due to *Actinomyces* are found on the jaw. (*See* p. 241, *General Pathology.*)

NECROSIS :—

This may result from the inflammatory conditions already noted, and usually starts as a periostitis. The lower jaw is more frequently and more severely attacked than the upper. Necrosis may be secondary to **injury** (especially to compound fracture), to some of the **acute infective fevers** such as measles, scarlet fever, typhoid fever or smallpox, to **syphilis,** to **cancrum oris,** or to the now comparatively uncommon conditions of **mercury** and **phosphorus poisoning.** In syphilis, the necrosis is sometimes very extensive, and the palatine process of the superior maxilla is extremely liable to be involved—the destructive change extending to the soft palate and fauces.

TUMOURS AND CYSTS :—

Reference has already been made to tumours and cysts of the teeth. Of the **tumours of the jaw,** the most important are the **sarcomas** and **carcinomas.** The **sarcomas** are usually of the round- or spindle-celled variety, and commence from the periosteum of the jaw and also in the anterior or posterior wall of the antrum. The cancers may be squamous-celled growths taking origin in the gum or palate, or of columnar-celled type commencing in the glandular tissue of the nasal or antral cavities. Tumours of the lips or of the tongue may spread so as to involve the jaws. Of the simple tumours, **epulis** is the commonest. **Myelomata,** which by some authorities are still classed as giant-celled or myeloid sarcomas, are situated usually in the lower jaw.

Chondromata, osteomata, and **fibromata** may be found.

DISEASES OF THE SOFT PALATE, PHARYNX, AND TONSILS

DIVERTICULUM OF PHARYNX.—This condition is unusual. The pouch springs from the posterior wall of the pharynx, its orifice being situated opposite the cricoid cartilage. It is produced by a gradual evagination of the mucous and the submucous coats of the pharynx between the two parts of the inferior constrictor muscle. The pouch is at first small, but gradually enlarges. The diverticulum may become filled with food, undergo further enlargement, and eventually come to press upon and obstruct the œsophagus.

INFLAMMATION :—

Processes of an inflammatory nature are the commonest and most important pathological phenomena in the soft palate, pharynx and tonsils, and, when acute, are frequently described under the term **angina.** They differ very little from inflammatory changes elsewhere, their special characters depending largely on the looseness of the structures and the presence, in this region, of a large amount of lymphatic tissue, which is distributed in the form of isolated rounded masses resembling the solitary follicles of the intestine. Congestion and œdematous swelling are usually marked features of such inflammation.

(*a*) **CATARRH,** in its acute form, is generally the result of invasion by organisms, e. g. *Staphylo-*, *Strepto-*, and *Pneumo-cocci*, *B. diphtheriæ* and *pseudo-diphtheriæ*, *B. influenzæ*, *M. catarrhalis*, etc.; though it may be caused, or a suitable nidus for these organisms be prepared, by irritation, *e. g.* by hot liquids, chemicals, exposure to cold, etc. It is particularly common in acute infections—many of the infective diseases having, for their first sign, " sore throat " or **pharyngitis.** The mucous membrane becomes reddened and swollen, and, at a later period, is covered with a mucous exudate. Sometimes small vesicles may develop, and these, by their rupture, may lead to ulceration.

(*b*) **CHRONIC CATARRH** may follow repeated acute attacks, and is of frequent occurrence in people who use the voice excessively, and in smokers. In the earlier stages, the mucous membrane is thickened; but, later, it may become indurated and atrophic. " Granular " elevations are frequently seen, these being either distended mucous glands or proliferated lymph-follicles. The term **granular pharyngitis** has been applied to this condition.

(*c*) **ACUTE PHLEGMONOUS PHARYNGITIS.**—In this condition, the mucous membrane and the submucous tissues are involved in an acute inflammation, which, later becomes **suppurative.** The soft palate, uvula, tonsils, and other adjacent structures, may be much swollen, deeply congested, and œdematous. The œdema often extends to the loose structures of, and around, the epiglottis, and sometimes **œdema glottidis** may supervene. The disease is almost always bacterial in origin,

various forms of *Streptococci* having been most frequently isolated from such cases. Other bacteria, however, may also produce the condition. **Retropharyngeal abscess** may follow, but this may also be a sequel of certain of the infective fevers, tuberculosis of the faucial or pharyngeal mucous membrane, tuberculous caries of the spine, or, in some cases, degenerative and suppurative changes in the retropharyngeal glands.

(*d*) **VINCENT'S ANGINA.**—This is an acute inflammation of the pharynx and tonsils which may be characterised by the formation of a firm yellowish-white false membrane, very similar to that seen in diphtheria. All degrees of ulceration may occur. In some cases, it is merely superficial, whilst, in others, usually accompanied by extensive œdema, it may be the most prominent feature, and a soft, necrotic, foul-smelling membrane may be produced.

Similar ulcerative and membranous conditions may be found on the
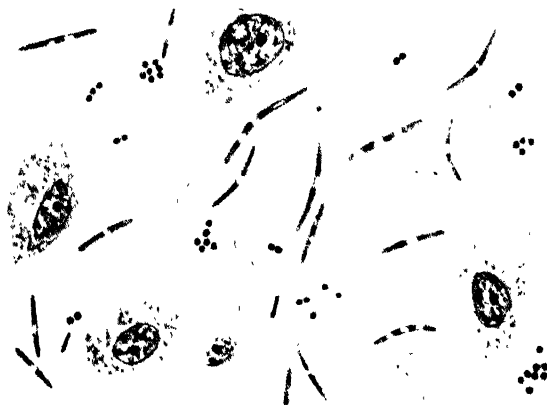
Fig. 340.—*Vincent's Angina.* Film from exudate of ulcer on tonsil, shewing spirochætes, *B. fusiformis*, etc. × 1000.

cheeks, gums or palate, giving rise to necrotic inflammations, ulcerative stomatitis and noma. The association of *B. fusiformis* with this special type of inflammation was first recognised by Vincent. *Spirochætes* are always present, and Tunnicliffe regards these spirochætes as stages in the development of the fusiform bacillus. This relationship is not proved. It has been frequently shewn that both *B. fusiformis* and the *spirochætes* may be found in the secretions of the mouth in normal conditions, and may be present in considerable numbers in cases of true diphtheria. Similar organisms are found in catarrhal and other inflammatory conditions of the mouth and fauces. They are often found in the tonsillar crypts, with or without inflammatory changes.

(*e*) **DIPHTHERIA** usually begins in the mucous membrane of the tonsils, and may spread to the fauces, the uvula, the posterior wall of the pharynx, and to the nares, the larynx, and the trachea, and even, in rare instances, down the œsophagus. At first, the tissues of the fauces are

hyperæmic and swollen. Later, greyish or yellowish spots, somewhat resembling wash-leather, make their appearance, and generally coalesce into a definite **false membrane.** The underlying tissues become infiltrated with inflammatory exudate, and, when the false membrane is removed, a raw, bleeding surface, with varying degrees of necrosis is seen. **On microscopical examination,** the false membrane is found to consist of necrotic mucous membrane and masses of fibrin, entangling leucocytes and degenerated epithelial cells. On the surface, there are accumulations of débris, containing large numbers of organisms, especially various kinds. of cocci, in addition to *B. diphtheriæ* itself. In the later stages of the disease, there may be extensive necrosis of the mucosa and submucosa. The causal organism is *B. diphtheriæ.* Associated with the inflammatory reaction in the pharynx, there is frequently some enlargement of the lymphatic glands at the angle of the jaw and elsewhere in the neck. In some cases, this swelling may be very severe, and is generally associated with the presence of *Strepto-* or *Staphylo-cocci* in these structures.

(*f*) **TONSILLITIS** may be acute or chronic. In the **acute** form, the surface is usually marked with small whitish spots, which are produced by the degeneration of the epithelium in the lacunæ or crypts of the tonsil. There is in addition, inflammatory swelling of the tissues; and ulceration or suppuration may supervene in the tonsil itself, or, more frequently, in the alveolar tissue of the soft palate above the tonsil, giving rise to the peritonsillar abscess or quinsy. In the **chronic** form, the tonsils are, in most cases, enlarged, both from hypertrophy of the lymphatic follicles and from increase in the interstitial connective tissue. This chronic proliferative overgrowth is due to repeated acute or subacute attacks. Pressure on the lacunæ may cause obstruction and retention of the contents, which sometimes become inspissated, and even calcified. **Tonsillar calculi** so formed are usually small, but, in a recent case, seen by one of the authors, a calculus about the size of a walnut was removed by operation.

In association with this chronic enlargement of the tonsils, there is frequently proliferation of the lymphoid follicles of the pharynx. To this condition—especially when occurring in the roof of the pharynx in young subjects—the term **adenoid growths** or **adenoids** has been given.

GRANULOMATA :—

SYPHILIS.—As in the mouth, mucous patches or condylomata may be present. In the **tertiary** stage, there may be necrosis and ulceration of the mucous membrane, etc., with or without the formation of gummata. This necrosis and ulceration may cause extensive destruction of the uvula and soft palate—often with **perforation** of the latter—and may be accompanied by interstitial overgrowth and subsequent cicatricial contraction.

TUBERCULOSIS.—Tuberculous ulceration in the pharynx is, with few exceptions, secondary to tuberculosis of the lungs or of the larynx; but

a tuberculous affection of the tonsils may occur as a primary condition, owing to invasion of the crypts by the bacilli, and is a comparatively common lesion, especially in children in certain districts. In tuberculosis of the cervical and submaxillary lymphatic glands, it appears that the infective material frequently obtains entrance by way of the tonsils, the small lymphatic gland lying immediately behind the angle of the jaw, through which the lymph-return from the tonsils takes place, being, as a rule, the first to become affected (Dowden).

TUMOURS.—Sarcomata, which often commence as polypi, are found in the naso-pharynx; and the tonsils may be the seat of **lympho-** and of **mixed-cell sarcomata.**

Squamous epithelioma may occur in the tonsil and also in the region of the epiglottis, but is almost always a secondary involvement.

Endotheliomas in the naso-pharynx and in the tonsils have been described.

DISEASES OF THE SALIVARY GLANDS

INFLAMMATION :—

Of these organs, the parotid gland is the most frequent seat of pathological change. **Inflammation** of the gland **(parotitis)** may be an independent infection **(acute infective parotitis,** or **mumps),** or it may be secondary to such infectious diseases as typhoid or typhus fever, etc. The gland becomes swollen and very tense. In the primary affection, suppuration very rarely occurs; but it is not infrequent in the secondary conditions, which are generally caused by infection from the mouth. The specific organism of mumps is not definitely known, but several observers have isolated a diplococcus which they consider causal. A lymphocytosis seems to be a constant feature of the cerebro-spinal fluid, and meningitis or meningeal irritation is not infrequent. **Acute orchitis, ovaritis,** and **mastitis,** and also, it is said, **pancreatitis,** are occasional complications of mumps. Abscess formation in the parotid sometimes supervenes in pyæmia.

Intense inflammatory reaction **(Angina Ludovici),** often with abscess formation, occurs occasionally in the floor of the mouth, and in the tissues round the submaxillary gland, *e. g.* in cases of scarlet fever. A similar condition sometimes results from the spread of carious and suppurative processes at the roots of the teeth.

SALIVARY CALCULI are commoner in the submaxillary and sublingual glands than in the parotid. They are usually produced by a deposit of lime-salts in the thick mucous secretion and desquamated cells following inflammation of the ducts, and are generally single, but may be multiple. Such calculi may be formed in the ducts either within, or external to, these glands.

GRANULOMATA.—Tuberculosis, Syphilis, and **Actinomycosis** are rare in the salivary glands, but cases of each have been recorded.

MICKULICZ'S DISEASE.—In this condition, there is a symmetrical enlargement of the salivary and lachyrmal glands—and, in some cases, of the labial and buccal mucous glands. The enlargement begins in early adult life and is progressive. Some authors regard it as a granuloma, while others consider it lymphadenomatous. No relationship to syphilis or tuberculosis has been demonstrated.

TUMOURS AND CYSTS :—

Cystic dilatation of the salivary ducts, sometimes with the presence of **concretions** or **calculi in the ducts,** is seen giving rise to oval or rounded swellings containing somewhat viscid fluid (*see* pp. 344 and 737). **Tumours** are rare, but **fibromata, lipomata, hæmo-** and **lymph-angiomata,** and **chondromata** are found. The commonest tumour in the parotid gland is one which is composed of a mixture of adenomatous tissue and cartilage in which myxomatous degeneration is very liable to take place- -the so-called **myxo-chondro-adenoma.** Similar tumours may also be found in other salivary glands. **Sarcomata** and **carcinomata** occur.

DISEASES OF THE ŒSOPHAGUS

DEVELOPMENTAL ABNORMALITIES, MALFORMATIONS, etc. : —

· **Communication of the œsophagus and trachea.**—The lower part of the œsophagus may spring from the posterior wall of the trachea and may not be connected with the upper part of the gullet, which, in such cases, ends blindly at a point some distance above the bifurcation of the trachea. The opening of the trachea into the lower part of the œsophagus is usually about the junction of the upper three-fourths with the lower fourth. The condition is incompatible with life, and is due to a mal-development of the septum between the œsophagus and trachea.

An anterior diverticulum of the œsophagus is sometimes found near the bifurcation of the trachea, opposite the site of the bronchial glands. Such diverticula are usually small and conical, and, according to some writers, they are caused by traction on the œsophagus by adhesions which are formed between it and diseased bronchial glands. Ulceration and perforation may supervene, giving rise to septic infection of the pleura, pericardium, or lungs.

Dilatation of the œsophagus, generally towards its lower part, gives, in extreme cases, the appearance of the presence of an accessory stomach. In some instances, this seems to be a congenital condition due to hypertrophic stenosis of the lower œsophageal sphincter.[1] A considerable degree of dilatation of the œsophagus, especially in its lower half or two-thirds, is usually found in cases of congenital pyloric stenosis, and is, as a rule, combined with well-marked hypertrophy of the wall. General dilatation of the œsophagus may occur in cases of stricture of the cardiac orifice of the stomach, *e. g.* from tumours or other causes.

[1] *See* footnote, p. 748.

CIRCULATORY DISTURBANCES :—

CHRONIC VENOUS CONGESTION of the mucous membrane is found in **diseases of the heart or lungs,** or in cases of **cirrhosis of the liver.** In the latter condition, owing to obstruction of the circulation through the portal vein, the œsophageal veins at the lower end of the tube become varicose, and the mucous membrane over these varicosities may undergo ulceration. The ulcers are usually small and terraced, and they sometimes open into the veins and give rise to serious, and even to fatal, hæmorrhage.

INFLAMMATORY and NECROTIC CONDITIONS :—

Inflammatory changes of a more or less severe character, with necrosis of the mucous membrane, may result from the ingestion of corrosive acid or alkaline liquids, from scalding, or from the impaction of foreign bodies, such as tooth-plates, bones, etc., in adults, and safety-pins, coins, the bone-plates of babies' teats, etc., in children. In these cases, ulceration and perforation, giving rise to abscess-formation, cellulitis, pleurisy, or empyema, may supervene. **Ulceration** is sometimes found in cases where the cause is as yet unknown. Pringle and Teacher [1] report several cases of post-operative hæmatemesis, in which lesions, varying from superficial erosion of the interior of the œsophagus to perforation or wide-spread destruction of the tube and damage to adjacent structures, were found. They state that : " the vital nature of the condition is shewn by the presence of hæmorrhages into the œsophageal wall, lungs and pleuræ," and that, in one case, " inflammatory action was observed in the lungs and pleural sacs." They conclude that digestion of the œsophagus may occur during life and be one cause of post-operative hæmatemesis. If there has been severe damage, with considerable loss of substance, during the inflammatory or ulcerative process, **cicatricial contraction,** producing **stenosis,** may be a result of the excessive reparative processes in the damaged area. Thus, one or more localised fibrous **strictures** may be formed.

POST-MORTEM DIGESTION of the lower end of the œsophagus is very common, and all degrees of change, from superficial erosion of the lining cells to actual perforation, are seen. The absence of inflammatory reaction in this condition serves to differentiate it from pathological changes produced during life.

STENOSIS of the œsophagus, resulting from the **cicatricial strictures,** has been referred to above. Contraction of the upper end of the œsophagus may also be due to a special tonicity of the upper sphincter; or to a fibrous replacement of the muscle-fibres in that sphincter, and a definite fibrous stricture may be present. Congenital stenosis of the mid-part of the œsophagus—from the bifurcation of the trachea to within one or two centimetres of the diaphragm—has been described. Stenosis is sometimes due to pressure by aneurism. Malignant stricture

[1] Pringle and Teacher, *British Journal of Surgery,* Vol. VI., No. 24. 1919, pp. 524 *et seq.*

will be dealt with under tumours of the œsophagus, as will also the secondary phenomena produced in the œsophagus itself by such constrictions. In many cases in which there has been marked clinical evidence of obstruction during life, little or no narrowing of the œsophagus is found after death. Such cases are due to irritative muscular spasm, or, in some instances, the phenomena have been of purely nervous origin.

TUMOURS :—

The occurrence of **fibromas, lipomas,** and **myomas** has been described, but these tumours are all very rare. **Papillomas** are commoner.

The most important tumour of the œsophagus, however, is **carcinoma.** The growth is, in nearly all cases, a **squamous-celled epithelioma.** A tumour of this nature may occur in the pharynx or in any part of the œsophagus, and, though its most usual situation is the upper third, it is almost as often found in the middle third, where the left bronchus crosses the œsophagus. Starting at one point, it spreads circularly round the wall of the tube, the growth being localised, or spreading widely, and infiltrating first the mucous and submucous coats, and, later, invading the deeper parts. Dilatation of the tube, with hypertrophy of its wall, may occur above the tumour, if obstruction is present; but, even with comparatively large, projecting tumours, there may sometimes be little or no obstruction. In some cases in which the opposite wall of the œsophagus lies in contact with the tumour, " **contact** " epitheliomata develop. Ulceration may take place, and communication between the œsophagus and the surrounding parts be established. The glands in the neighbourhood may be secondarily infected, and, occasionally, small metastases are found in the pericardium.

Glandular carcinomata and also **sarcomata,** are extremely rare as primary growths; but the extension of a tumour from the stomach, coming to involve the œsophagus, is not uncommon.

DISEASES OF THE STOMACH

In studying diseases of the stomach, it is important to remember that interference with its normal structure will cause derangement of its function, and that this will aggravate the pathological condition which is present. Thus, any disease of the stomach will interfere with the function of the gastric glands, and the contained food will remain imperfectly digested, and will undergo decomposition-changes. The products of such decomposition—acetic, lactic, butyric acid, etc.—cause further irritation of the mucous membrane, and the gases formed during the process produce distension of the viscus and interference with its peristalsis.

POST-MORTEM CHANGES :—

Decomposition-changes in the food-contents of the stomach occur **very soon after death;** and the decomposition-products, acting on the mucous membrane, cause it to assume a reddish or greenish colour,

which, later, becomes slaty-blue or almost black, owing to chemical altera-
tions in the blood-pigment. Thus, vascular and other changes which
may have been present during life are often obscured.

In some cases in which death has taken place while the processes of
digestion are proceeding, or while the secretion of gastric juice is active,
digestion of the coats of the stomach itself is observed. In this
condition of **post-mortem digestion** or **cadaveric softening,** the mucous
membrane becomes swollen, softened, and digested away, and the muscular
and peritoneal coats may become perforated. This *post-mortem* change
is, as a rule, found in the neighbourhood of the fundus, generally on the
posterior wall near the cardiac end—that is, in the situation on which
the stomach contents lie when the body is in the dorsal position. The
softened area is frequently extensive, its edges are usually much thinned—
sometimes resembling tissue-paper—and may be shred-like, and there
is no evidence of any inflammatory action in the neighbourhood. The
stomach-contents are sometimes found free in the peritoneal cavity.
The condition is differentiated from *ante-mortem* perforation or rupture of
the stomach by the absence of peritonitis, and of any thickening or inflam-
mation at the margin of the perforation, but it must always be remembered
that *post-mortem* digestion may be superimposed on actual pathological
conditions and give anomalous appearances.

MALFORMATIONS :—

(*a*) **HOUR-GLASS CONTRACTION** of the stomach is a moderately
common condition, the contraction being situated usually about the
middle of the organ. There is no doubt that, in the majority of cases,
this is due to chronic inflammatory and cicatricial changes following
ulceration, or to infiltration and contraction produced by carcinomatous
tumours. More rarely, it is caused by the contraction of peritonitic
thickening or adhesions on the outer wall of the organ. There are,
however, cases in which the condition is apparently due to the permanent
contraction of the so-called mid-gastric sphincter, which, according to
various observers, is usually only active during digestion, and marks the
boundary between the cardiac and pyloric portions of the stomach.

The condition of hour-glass contraction of the stomach should be
carefully differentiated from stricture in the duodenum with dilatation
of its first part.

(*b*) **ATRESIA,** or complete closure of the pylorus is rare, but
CONGENITAL HYPERTROPHIC PYLORIC STENOSIS is not uncommon.
In this latter condition, which occurs especially in very young children
—though it may also persist in adults—there is marked hypertrophy of
the muscular layer, particularly of the circular-fibres of the pylorus, and
there is usually associated dilatation and hypertrophy of the œsophagus,
especially towards its lower part. Hypertrophy of the cardia [1] (with

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[1] Proceedings of the *Royal Society of Medicine*, Vol. XIII, No. 5, March, 1920,
p. 43.

dilatation of the œsophagus above it), and of the ileo-cæcal sphincter, has also been described as occurring in some cases, in association with congenital pyloric stenosis, as well as independently of that condition. Various explanations of these localised hypertrophies of the gastro-intestinal sphincters have been suggested, such as inco-ordination from abnormalities of innervation, etc., and some recent writers (Pirie, Tyrrell Gray, and others) are of opinion that the condition may be due to hyperadrenalism, either on the part of the child itself, or of the mother.[1]

MALPOSITIONS :—

ANTERIOR DISPLACEMENT on account of defects in the anterior abdominal wall may occur. **DOWNWARD DISPLACEMENT** or **GASTRO-PTOSIS** is commoner, and may be congenital, or the result of **dilatation** of the stomach, or of **traction** on it by inflammatory adhesions. In cases with **TRANSPOSITION OF THE VISCERA,** the stomach may have its position reversed, the cardiac end of the organ being towards the right side (*see* fig. 341).

CIRCULATORY DISTURBANCES :—

(*a*) **ACUTE CONGESTION** is seen as an early stage of inflammation of the mucous membrane, or it may be transitory

(*b*) **CHRONIC VENOUS CONGESTION or PASSIVE HYPERÆMIA,** as a *post-mortem* phenomenon, is comparatively common. This condition may arise secondarily to obstructive disease of the heart, but especially as a result of obstruction of the portal circulation by cirrhosis and other diseases of the liver. The mucous membrane is reddened and œdematous, and minute hæmorrhages are frequently found in the submucous tissues. Over these hæmorrhages, the mucous membrane generally becomes eroded, possibly by being digested by the gastric juice, and small ulcers—**hæmorrhagic erosions**—being produced. These hæmo-rrhages and erosions may be present in considerable numbers, especially towards the pyloric end. After healing, they may be represented by small areas of **atrophy.** Chronic catarrhal changes are usually also present in such çases.

(*c*) **HÆMORRHAGES** in or from the mucous membrane arise

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[1] Tyrrell Gray, "Discussion on Hypertrophic Pyloric Stenosis with Associated Hypertrophies," *Royal Society of Medicine Transactions,* Children's Section, Vol. XIII., No. 5, March 1920, p. 37. "As to why other parts of the bowel have not hypertrophied, the explanation is a simple one: the sympathetic supply to the intestine is inhibitory to circular muscle, and Elliott has shewn that reversed innervation takes place in the sphincter areas in the intestine. Any stimulus, therefore, which inhibits the bowel muscle will cause a concurrent spasm of the sphincter areas. Sympathetic nerve endings in involuntary muscle are acted on by both nerve stimuli and suprarenal hormone. Hence hyperadrenalism would inhibit the contraction of the circular muscle except at the sphincters, when spasm would result. . . . I do not see how true hypertrophy could occur except by over-action, and there must be some general cause which produces the over-action. No better explanation of such over-action has, I think, been offered than Dr. Pirie's suggestion of hyperadrenalism." Tyrrell Gray is also of opinion that minor degrees of pyloric hypertrophy often occur undetected

from a variety of causes. Simple gastric ulcers, or cancerous infiltration, by invading and opening into vessels, may give rise to any degree of bleeding, from general oozing of blood up to very severe hæmorrhages. In acute yellow atrophy of the liver (acute liveratrophy), purpura, scurvy, septicæmia, hæmophilia, and some of the acute fevers, e.g. yellow fever and typhus : in chloroform- and phosphorus-poisoning, and in severe forms of anæmia and other " blood-diseases," hæmorrhage results, probably from fatty or other degenerative changes in the vascular endothelium, with subsequent rupture

Fig. 341.—*Transposition of Viscera.* Note apex of heart on the right side, stomach on the right side, the cæcum and appendix are transposed to the left side. Note also the double thumb on the right hand. (From a case of the late Sir Thomas R. Fraser.)

of minute vessels. In certain forms of cardiac disease, and in cirrhosis of the liver, rupture of the distended veins, or ulceration over and extending into them, may lead to hæmorrhage. In the condition known as **Gastrostaxis,** there is said to be an oozing of blood from the mucous membrane of the stomach, not only in the absence of any ulceration of that organ, but also in the absence of any other disease in which bleeding is likely to occur. We have not encountered any such case in the *post-mortem* room, and a very careful examination of the whole

mucous membrane would require to be made before a diagnosis of gastrostaxis could be established.

Except in cases where an ulcer has opened into a comparatively large vessel, in which case pure blood may be vomited, the escaped blood becomes mixed with the contents of the stomach, is dark brown or almost black in colour, and is vomited in a semi-digested condition (" coffee-ground vomit ").

INFLAMMATION (GASTRITIS) :—

On account of the stomach being so much exposed to irritation, **gastritis,** in varying degree, is very common. The **acute** form is apt to occur in connection with many of the acute infective fevers, from the swallowing of irritant poisons, or even after mere exposure to cold ; or it may be due to surfeit, or the ingestion of irritating and indigestible foods. If the condition is severe, the mucous membrane becomes swollen, reddened, and softened, and shews minute hæmorrhages, or even hæmorrhagic erosions, especially towards the pyloric end. It is covered with viscid, tenacious, and perhaps blood-stained, mucus. When due to the ingestion of irritant poisons, the inflammatory reaction is most marked along the prominent parts of the rugæ, or where the stomach-walls are in contact with one another. The mucous membrane is discoloured, **nitric acid** giving a **green, sulphuric acid** a **black,** and **carbolic acid** a **dark brown colour.** Necrosis may occur and lead to perforation of the stomach ; or there may be swelling, hæmorrhage and membranous inflammation with ulceration. These conditions are often well marked in cases in which large doses of arsenic or mercuric bichloride have been taken by the mouth.

(*a*) **PHLEGMONOUS or DIFFUSE SUPPURATIVE GASTRITIS** is not of frequent occurrence. In it there is intense redness and swelling of the mucous membrane, due to acute inflammatory changes, which terminate in a diffuse infiltration of the mucous and submucous tissues with pus. Sometimes, minute abscesses form, and these may rupture into the cavity of the stomach. The condition may start from an ulcer, but, as a rule, its origin is obscure. It is generally associated with the presence of one of the varieties of *Streptococci.*

(*b*) **CHRONIC CATARRH** very frequently results from repeated acute attacks, or it may be due to improper feeding. It is a usual sequel of chronic venous congestion and other diseased conditions of the stomach, and, in many cases, is caused by the swallowing, over prolonged periods, of infective material from the nose, mouth, or throat.

The stomach is usually more or less dilated. There is general thickening of the mucous membrane, and towards the pyloric end this thickening is often very irregular, and the surface may present a mammillated, or even a warty, appearance. The mucous membrane is reddened and hyperæmic, and usually shews irregular, pigmented patches of a slaty-blue colour—this pigmentation being caused by changes produced

in the blood in the hæmorrhagic areas. Covering the mucous membrane, there is usually an excess of viscid mucus. If the catarrhal condition is prolonged, there generally occurs a new formation of connective tissue, together with atrophy of the various glandular structures. The overgrowth of connective tissue causes obstruction of the orifices of the ducts, and the production of small cysts. There is frequently hypertrophy of the muscular coat. From the stagnation and decomposition of the gastric contents, various general toxic phenomena are produced, amongst the rarest of which may be noted the occurrence of **gastric tetany.**[1]

ULCERATION OF THE STOMACH :—

1. **FOLLICULAR ULCERS,** from $\frac{1}{8}$- to $\frac{1}{4}$-inch in diameter, are frequently seen in chronic gastric catarrh, especially in alcoholic subjects, and also in phosphorus-poisoning. They are usually shallow, and at first have undermined edges. Several of them may coalesce, forming an irregular ulcer which is often described as the **alcoholic ulcer.** On healing, this may leave a puckered scar.

2. **ACUTE ULCER.** Acute ulcers of the stomach, apart from the small follicular ulcers already described, are not common, but several observers have described cases where, at the *post-mortem* examination, numerous acute ulcers were found scattered widely over the mucous membrane. They are usually superficial—the base of the ulcer being the deeper part of the mucous membrane. The tissues in the immediate neighbourhood may shew polymorphonuclear leucocytic infiltration.

3. **SIMPLE GASTRIC OR PEPTIC ULCER.**—This form of ulcer is common, especially in young women, and is caused probably by the direct action of the gastric juice on a part of the stomach-wall which has been damaged. Various hypotheses have been put forward to account for the production of this damage. Thrombosis of one or more of the small arteries may account for some of the ulcers. Bolton has brought forward much evidence in favour of the view that the destruction of tissue is caused by the action of the gastric juice on areas of the mucous membrane which have been damaged by toxins circulating in the blood. There is abundant evidence that acute ulcers are developed during the course of infective disease, and experimental evidence also shews that the ulcers are acute and that healing takes place rapidly. There is no doubt that certain substances introduced in excess with the food may also act as protoplasmic poisons. Motor insufficiency, *i. e.* inability of the stomach to get rid of its contents in normal fashion, delays the healing of the ulcers, and this delay means a continuance of the irritation which causes thickening at the base of the ulcer and less complete regeneration of the gastric glands. Such motor insufficiency is certainly present in many of these cases in which gastric ulcer is found, and the view put forward by Bolton seems a very reasonable one. As he points out, if

[1] *See* Carnegie Dickson, " Gastric Dilatation and Tetany," *The Practitioner,* Vol. LXX., No. 1, January 1903, p. 44.

this motor insufficiency is lessened or removed by gastro-enterostomy, even chronic ulcers tend to heal. Further, it has been shewn by various observers that the ulcers which form in the jejunum after gastro-enterostomy occur in cases where the opening into the jejunum is too small or has become stenosed, or in cases where there has been obstruction by twists, etc. Hyperacidity of the stomach-contents may play some part in the production of these ulcers, but of itself is not sufficient to cause them, as has been shewn experimentally by Urekie. There must be, in addition, some injury to the mucous membrane, and this may be produced by irritant foods. In Türck's experiments, mechanical and chemical irritation failed to produce ulcers, but he was able to

Fig. 342.—*Simple Ulcer of the Stomach.* Shewing the terraced appearance and oval shape. There is perforation into the splenic vein. (A rod is placed in the vein.) (Edinburgh University Anatomical Museum. Catalogue No., Al. D. d. 3.)

produce them by feeding dogs with *B. coli.* He says: " The factors concerned in the production and persistence of ulcer of the stomach and duodenum appear from the experiments to indicate a dual condition : there seems to be some toxic condition produced, which overcomes natural resistance, resulting in *cytolysis,* and possibly some chemical substance formed within the alimentary tract, which, when absorbed, may neutralise the protective bodies in the blood and tissues, resulting in *autocytolysis.*"

Rosenow [1] states that " the ulcers produced by the injection of streptococci resemble those in man in location, in gross and microscopic appearance, and in that they tend to become chronic, to perforate and to cause a severe or fatal hæmorrhage "; and he considers that the usual ulcer of the stomach and of the duodenum in man is primarily due to

[1] Rosenow, *Jour. Infect. Diseases,* 1916, xix. pp. 333–4.

a localised hæmatogenous infection of the mucous membrane by streptococci.

A similar ulcer may occur in the first part of the duodenum (**Duodenal ulcer**), and in the jejunum, and, it is said, also in the lower part of the œsophagus. The commonest situation—*i. e.* in about sixty-five per cent. of the cases—is on the posterior wall of the stomach, on, or close to, the lesser curvature. The ulcer may also occur at the pylorus (twelve per cent.), on the anterior wall (eight per cent.) and on the cardia, the fundus and on the greater curvature.

, **Characteristics of the Ulcer.**—It is more or less oval or circular in

Fig. 343.—*Simple or Peptic Ulcer of Stomach.* Section of the edge shewing the smooth floor, etc.   × 5.

shape, at first limited to the mucous membrane and very sharply defined, the edges being slightly sloping or bevelled, and the floor at first smooth. There is usually little or no evidence of surrounding inflammation. The ulcer may spread acutely, but usually it tends to become chronic, and to extend more deeply into the submucous and muscular coats, the ulcer having a terraced appearance, wider on the inner or mucous surface of the stomach-wall, and—if perforation has taken place—narrowing, perhaps, to a minute orifice, through which communication with the peritoneal cavity or some of the abdominal organs may be established (fig. 342). The ulcers are usually single, but, in some instances, several are present.

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Effects of the Ulcer :—

(a) **Hæmorrhage.**—Erosion into one of the branches of the coronary or other vessels of the stomach or into the splenic vein may take place; or the rupture of a minute aneurism on one of the small gastric vessels in the base of the ulcer may lead to severe, or even fatal, hæmorrhage. In cases of erosion into the pancreas, the splenic artery may lose its support and an aneurism be developed on it, which may rupture and lead to fatal hæmorrhage.

Fig. 344.—*Simple or Peptic Ulcer of Stomach.* Section of base, shewing granulation-tissue which was densely infiltrated with eosinophil cells. × 75.

(b) **Perforation** is commoner in ulcers of the duodenum than in those of the stomach, and, where, in the latter, rupture does take place, the ulcer is generally found in the anterior wall. Generally, the wall of the ulcerated stomach becomes more or less adherent to the liver or the pancreas, or, more rarely, to the spleen, the diaphragm, the colon, or the abdominal wall, and thus rupture into the peritoneal cavity is prevented. After adhesions have been formed, the ulcer may burrow into the various organs or tissues to which it is adherent, the eroded pancreatic or liver-tissue, etc., coming in this way to form the floor of the ulcer. The cavities thus produced sometimes become the sites of septic

infection, and acute septicæmia may be a later result. Perforation into the pleural cavity, into the lung or a bronchus, and into the pericardium is sometimes a sequel.

(c) **Stricture.**—The ulcer, when situated at or near the pylorus, frequently leads to stricture, with partial, or sometimes almost complete, obstruction. When further from the pylorus, such constriction may produce the condition known as **hour-glass contraction of the stomach** (see p. 747). Peristalsis is delayed, dilatation and perhaps a considerable degree of hypertrophy of the stomach above the constriction take place, whilst other ulcers form behind the constriction.

(d) **Healing of the Ulcer** is a very usual occurrence, flat cicatrices being produced which may lead to considerable contraction and puckering of the surrounding stomach-wall. In the granulation-tissue at the base of such ulcers, numerous eosinophil cells are sometimes found (fig. 334). If the ulcers are near the pyloric ring, the cicatricial contraction may, as already mentioned, lead to the production of marked **stenosis.**

(e) **Cancer.**—Many observers hold that cancer of the stomach results from, and commences at the site of, a chronic ulcer. It is difficult to establish this, but many cases of cancer have a definite history pointing to a previous chronic gastric ulcer. Wilson and MacCarty, at the Mayos' clinic, examined 153 cases of cancer removed by operation, and state that 109 of these shewed naked-eye and microscopical evidence that carcinoma had developed from pre-existing ulcers.

DILATATION AND HYPERTROPHY :—

These conditions generally result from obstruction to the passage of food through the pylorus; but dilatation may also result from accumulation of gas derived from bacteria, etc., causing the putrefactive changes which are frequently associated with chronic gastritis — the inflammatory condition of the stomach no doubt aiding, by lessening peristalsis and weakening the muscular wall.

Acute dilatation is said to occur frequently after a severe shock. This so-called " **idiopathic dilatation** " is supposed to be due to an interference with the nervous mechanism of the organ. An extremely important form of such acute dilatation is sometimes found following operations, especially those on the abdominal cavity. As a result of the dilatation, the greater curvature is displaced downwards, and sometimes the pylorus is depressed.

The muscular wall of the stomach, in cases in which the pylorus is obstructed, undergoes hypertrophy, which is specially marked at the pyloric end, but may involve the whole organ and even the œsophagus, especially in infants with congenital hypertrophic pyloric stenosis.

ATROPHY AND DEGENERATIONS :—

Atrophy of the glands and gland-tubules is common in chronic gastritis; and, in cases of obstruction in the œsophagus or at the cardiac

orifice of the stomach, atrophy may also occur. In starvation and in wasting diseases, the stomach-wall may shew marked atrophic thinning.

Fatty degeneration of the cells of the glands and gland-tubules, and of the vascular endothelium, results from acute or chronic poisonings, whether of an organic or inorganic nature. This condition is seen especially in phosphorus-poisoning, in septicæmia, and similar conditions.

Fig. 345.—*Encephaloid or Soft Cancer* at the cardiac end of the Stomach immediately below the opening of the œsophagus. (Edinburgh University Anatomical Museum. Catalogue No., Al. D. g. 1.)

Waxy or **Amyloid Degeneration** is rarely found in the blood-vessels of the mucous and submucous coats of the stomach.

GRANULOMATA :—

TUBERCULOSIS and SYPHILIS rarely produce any characteristic local lesions in the stomach, though in some cases of advanced pulmonary tuberculosis, especially in children, the occurrence of tuberculous ulceration of the stomach has been described. Ulceration, even with perforation, has been described as resulting from syphilis, but the more usual sequel is stricture either at the pyloric or cardiac orifice.

TUMOURS

Fibromas, myomas, lipomas, and simple **adenomas** are occasionally found. **Sarcomas** are rare, and, when present, are generally of the small round-celled type, especially lympho-sarcomas.

Carcinoma is the commonest and most important form of tumour of the stomach. It occurs generally in the later periods of life, and is commoner in the male than in the female. The most frequent sites are the pyloric end of the stomach and the lesser curvature, though it may develop at the cardiac orifice or at some area in the body of the organ. About **sixty** per cent. of tumours are found at the pylorus or in its vicinity,

FIG. 346.—*Cancer of the Stomach.* A large fungating mass growing from the anterior wall and showing extensive ulceration. (Edinburgh University Anatomical Museum. Catalogue No., Al. D. g. 14.)

twenty per cent. at or near the lesser curvature, **ten** per cent. at the cardiac orifice, and **ten** per cent. at other parts of the stomach-wall.

The tumours are usually **adenomatous** in type, and frequently shew **colloid** or **myxomatous degeneration.** Those at or near the pylorus grow rather slowly, and, during their growth, a considerable amount of fibrous tissue is formed, with only a moderate degree of cellular proliferation, giving a tumour of the **scirrhus** type. In some of these cases, the fibrous tissue is so abundant that the cancer-cells are difficult to find, and it may be that some of the so-called fibrous strictures are really cancers in which the fibrous overgrowth has prevailed. Fibrous strictures of the pylorus, due to chronic inflammatory changes, occur,

and cases are not infrequently reported in which a large "tumour," supposed to be cancer, had been previously present and had disappeared after gastro-enterostomy. This disappearance is taken as proof that the mass was inflammatory. It is just possible that some of these cases may be carcinomata in which the fibrous overgrowth has isolated, and eventually destroyed, the cancer-cells. Carcinomas in the body of the organ and in the lesser curvature grow more rapidly, and may form irregular, fungating, cauliflower-like excrescences, projecting into the cavity (see fig. 346). These tumours are very cellular, and exhibit the type of malignant adenoma or sometimes encephaloid cancer.

Effects on the Stomach.—Cancer at the pyloric orifice causes a ring-like infiltration of the mucous and submucous tissues, and thus produces a stenosis of the orifice which leads to dilatation and hypertrophy of the organ, with stagnation of food and consequent fermentation-changes, these latter being aided by alterations in the normal secretions and the multiplication of various bacteria, yeasts, torulæ, etc.

Ulceration of the inner surface of the tumour, and hæmorrhage, are usually later manifestations. A tumour at the cardiac orifice is, as a rule, small, unless it is associated with, and a continuation of, a squamous epithelioma of the œsophagus. But, in this situation, the tumour is more liable to damage; and, therefore, ulceration is a common feature of the condition. Cancer of the body of the stomach frequently becomes ulcerated, and hæmorrhage is a common sign of the disease.

Method of Extension of Cancers of the Stomach.—The extension of the tumour takes place by an infiltration of the mucous and submucous coats, leading to general thickening of a considerable portion of the stomach-wall, or to the formation of irregular fungating outgrowths. These fungating masses are very vascular, and are easily damaged, and in them ulceration is extremely common. The infiltration may spread into the muscular and peritoneal coats, and, in rare instances, perforation may result. Occasionally, especially in slow-growing cases, the infiltrated and thickened stomach-wall may undergo great contraction, and may even come to form a narrow, thick-walled tube, somewhat resembling a piece of thickened intestine—the so-called "leather-bottle stomach." Secondary growths are common in the liver and in the peritoneum; and the lymphatic glands in connection with the stomach are usually involved. Infection of the mediastinal glands may occur, and it is not uncommon to find enlarged cancerous glands at the root of the neck in such cases. Occasionally, widespread secondary growths in bones, especially in the bodies of the vertebræ, but sometimes in practically every bone in the body, may supervene.

PLASTIC LINITIS. (Cirrhosis of Stomach : Fibromatosis of Stomach.)—This condition—if it exists apart from malignant disease—is rare, and consists of a diffuse thickening involving chiefly the submucous coat. It is a disease of adult life and commences usually about the pylorus,

Cases have been described by various authors, but some of these have been shewn by the later history to be malignant, producing secondary growths in the liver. Doubts have been expressed as to whether all these cases would not have been shewn to be malignant (the fibrous-scirrhus type) if a sufficiently exhaustive microscopical examination had been made.

DISEASES OF THE INTESTINES

CONGENITAL MALFORMATIONS :—

From a fault of development, part of the large or the small intestine may be **absent.** This condition is seen especially in the rectum, the lower part—the **proctodæum**—not having united with the portion above, so that the condition of **imperforate anus** is produced. In some cases, the rectum has been found to open into the urethra in males, and into the navicular fossa of the vulvar cleft in females, or to end in a fibrous cord at the base of the prostate or in connection with the vagina. There may, in other cases, be congenital narrowness and defective development, sometimes with complete occlusion, in the small intestine, especially in the duodenum and the lower end of the ileum, close to the ileo-cæcal valve; or there may be stenosis at the junction of the pelvic colon with the rectum.

The commonest malformation is a **Meckel's diverticulum.** This varies from a slight rounded bulge to a long tube-like pouch, which is most commonly some two or three inches long, and may be continued by a fibrous cord. In infants, it is found at from twelve to eighteen inches, and, in adults, at from two to three feet, above the ileo-cæcal valve. It possesses the same structure as the intestine, has usually a somewhat narrower calibre, and is in direct communication with it. This diverticulum arises from the imperfect closure of the omphalo-mesenteric duct, and is sometimes connected with the umbilicus, where, if not completely closed, it gives rise to a fæcal fistula. If the lumen in some part of its course becomes shut off, the dilatation which follows, as a result of the accumulation of secretion in this closed sac, may give rise to the formation of a cyst—the so-called **enterocystoma.**

Diverticula are not uncommon in old people—especially in those who are the subjects of visceroptosis—in the posterior wall of the duodenum near the termination of the common bile-duct. They are composed wholly of mucous membrane and are probably due to pressure or traction, as they occur at the weak points in the musculature of the duodenum, and may be mistaken at an operation or *post-mortem* for ulcers. Smaller **diverticula** are found in the duodenum, jejunum, or other part of the intestinal tract, and not infrequently have an aberrant portion of pancreatic gland at their apices, the presence of the latter in the intestinal wall forming a weak spot, at which pouch- or finger-like dilatations supervene. Fæcal concretions may be formed or may accumulate in these diverticula, and give rise to

inflammatory reactions and suppuration; and thus abscesses are formed in the tissues round, especially, the more fixed parts of the intestine, *e. g.* the rectum.   **Diverticula** or irregular pouches of mucous membrane of the intestine, particularly the colon, especially in the descending and sigmoid portions, are also found passing between the layers of the mesentery (*see* fig. 347), and inflammatory changes sometimes occur in them—a condition known as **diverticulitis.**   The presence of such diverticula has

Fig. 347.—Multiple Diverticula of the Intestine.

been demonstrated, in the living subject, by X-ray examination after a bismuth- or barium-meal.

TRANSPOSITION.—Occasionally, transposition of the intestines occurs without transposition of the other viscera.   Usually, however, it forms part of a more generalised transposition (*see* fig. 341).

DILATATION of a more or less uniform character may result from prolonged constipation, or from unknown causes, and is sometimes very extreme in degree.   In " **Hirschprung's disease,**" or **megacolon,** enormous dilatation of the pelvic colon and, in some cases, also of the iliac and

descending portions of the colon, occurs, usually along with hypertrophy of the circular muscle-fibres in the wall. In cases in which the condition has lasted for some time, considerable **fibrous hyperplasia** occurs, and, if scybalous masses are retained in the dilated bowel, numerous irregular **ulcers** of the mucosa may be present. The cause of the condition is not understood. Acute dilatation or distension of the intestine is a common manifestation in cases of inflammatory conditions in the abdomen, e. g. peritonitis.

HERNIA :—

This term has a very wide application, but, in the abdominal cavity, it is generally taken as applying to a protrusion of some part of the intestine, the omentum, or other portion of the abdominal contents, into a sac composed of a prolongation of the peritoneum. The two commonest forms are **inguinal** and **femoral hernias.** The former is a protrusion, usually of some portion of the intestine, of the omentum, or of both of these, through the external inguinal ring, the contents descending through the inguinal canal : or a protrusion directly forwards through the internal inguinal ring under the skin of the abdomen. Femoral hernias are especially common in women, and consist of a protrusion of some part of the abdominal contents through the femoral ring, the hernia shewing itself at the antero-internal aspect of the thigh, at the position of the saphenous opening. Hernias at the sciatic notch and at the obturator foramen, or into the perineum or the vagina, at the umbilicus, at the sites of surgical and other wounds, etc., need only be mentioned. Full descriptions of these will be found in textbooks of Surgery.

Ætiology.—Hernias may be **congenital** or **acquired.** In the **congenital hernia,** the sac consists of either the unobliterated umbilical process or the funiculo-vaginal process, of the testis in the male or the canal of Nuck in the female. The umbilical process may give rise to the sac of a congenital umbilical hernia, and the funiculo-vaginal to that of a congenital hernia of the vaginal process, or of the funicular process, or, more rarely, in the female, of a congenital hernia of the canal of Nuck. In the production of **acquired hernia,** two important factors come into play, viz. **undue pressure,** and **weakness of the supporting structures.** Hernias resulting from undue pressure most commonly arise as a consequence of severe muscular efforts, such as are involved in lifting heavy weights, constant coughing, etc. The contraction of the muscles of the abdominal wall exerts considerable pressure on the contents of the abdomen, the wall gives way at specially unsupported parts, and more or less of the contents are protruded.

Pathological Anatomy.—In the congenital forms, the intestines or other contents project into the pre-existent tubes or sacs of peritoneum already referred to. In the acquired forms of hernia, the sac is composed of stretched peritoneum. In rare cases, this may rupture or disappear, and no definite sac be present.

The sac usually acquires, by a chronic inflammatory process, adhesions to the structures among which it is protruded, and sometimes to its contents.

Contents of the Sac.—The parts most commonly protruded are some portion of the intestines and the omentum, but the sac may contain any part of the abdominal contents. The neck of the hernial protrusion is usually constricted, and this constriction may be so marked as to cause interference with the blood-supply to the contents. The most direct effect is obstruction of the veins, producing congestion and œdema. The protruded portion may become dark in colour. Later, arterial obstruction may take place, and this, if sufficiently complete, leads to the occurrence of gangrene. Obstruction to the onward passage of the contents of the bowel is another important consequence.

Internal Hernias are generally protrusions of parts of the abdominal contents into pre-existing pouches, or through normal or abnormal apertures. The two most important of these are—

1. **Diaphragmatic Hernia.**—The true diaphragmatic hernia is a protrusion into the chest of some of the abdominal contents, through one of the normal apertures, or through a part of the diaphragm which, by reason of defective development, is absent, has given way, or has been ruptured by mechanical injury. The contents of the hernial sac are most usually intestine, spleen, liver, or stomach.

2. **Retroperitoneal Hernia** consists of a protrusion into pre-existing peritoneal pouches, which generally lie behind the peritoneum, from which they are offshoots. The most important of these pouches is the paraduodenal fossa, which lies behind the last part of the duodenum, and arises at the junction of the duodenum and jejunum.

Post-operative Hernia.—Portions of intestine or omentum may find their way into stretched scars or imperfectly closed wounds resulting from operations in the abdomen.

STRANGULATION :—

Internal strangulation may be brought about by compression and obstruction of the intestine by fibrous peritoneal adhesions, by a persistent cord of a Meckel's diverticulum, by a twisting of the coils upon themselves **(volvulus)**, or by the passage of a loop of bowel through an abnormal opening in the mesentery or elsewhere. Dilatation of the intestine occurs above the seat of the obstruction; and congestion, hæmorrhage into the lumen of the bowel and perhaps into the peritoneal cavity, peritonitis, necrosis, gangrene, and perforation may result. Strangulation of the bowel in a hernial protrusion has already been described.

VOLVULUS may affect practically any part of the more mobile portions of the bowel, may even involve the cæcum when it possesses a mesentery, but is most frequently found in the pelvic colon. This portion of the intestine is attached by its two ends to a fixed point, and it sometimes twists round this as an axis—the upper loop generally turning round the

lower. The twisting causes obstruction; and the bowel above the con-striction becomes greatly distended; and, if the condition persists and does not at once lead to a fatal issue, the muscular walls may become hypertrophied. The constriction may be very marked, and may produce congestion, hæmorrhage, necrosis, and gangrene of the bowel and peritonitis, and rapidly cause death.

INTUSSUSCEPTION :—

This is a condition in which one part of the intestine is invaginated into the lumen of the immediately adjoining part. It may occur at any part of the bowel, the most usual site being at the ileo-cæcal valve,—the valve and the ileum being carried into the ascending portion of the colon. The invagination may be extreme, and the apex of the intus-susception may even present at the anus. Sometimes, but much less frequently, the invagination occurs in the small intestine. In whatever situation it takes place, it is always the upper part of the bowel which slips, or rather is drawn, into the lower; for it is by the peristalsis of the lower part, and the absence of peristalsis in the enclosed upper portion, that the invagination occurs. Once the condition has commenced, it may continue as long as the peristalsis lasts, and more and more of the intestine be thus invaginated. The mesentery is carried in with the intestine, and, by being dragged upon at one side, it may give to the bowel an oblique direction. The packing-in of the intestine, and the pressure on the mesenteric veins, cause congestion of the bowel, and, it may be, hæmorrhage into its coats, interference with its nutrition, inflammatory changes, and even gangrene. **Sloughing,** with general peritonitis, may result; or permanent adhesions may occur between the outer ensheathing part and the upper end of the included portion, and, in the latter case, the invaginated part may, by necrotic or gangrenous changes, become separated and be passed *per rectum*, the continuity of the bowel being restored, with the loss of this gangrenous portion.

" **Agony-intussusception.**"—Invaginations in the small intestine are frequently seen at *post-mortems*. They are very common in children, especially in intestinal cases, and are often multiple—as many as a dozen or more being not infrequently found. They are usually small, but occasionally may be two or three inches long. These shew no inflam-matory or congestive changes, are without adhesions and are easily undone on gentle traction. They are probably due to local interference with peristalsis during the death-agony, and are of no special pathological significance.

PROLAPSE OF THE INTESTINE :—

This is usually a prolapse of the lower part of the rectum and anal canal (**prolapsus ani**), due to a weakness of the sphincter and to constant straining. It is commonest in young children, but may occur in adults and is frequently associated with hæmorrhoids. In some cases, the

mucous membrane of the lower part of the rectum alone is protruded; whilst, in other cases, the upper, more movable part of the rectum may be invaginated into the lower part and then protruded. The exposed mucous membrane, if not immediately replaced, becomes inflamed; and ulceration, hæmorrhage, and necrosis may subsequently result.

ATROPHY AND HYPERTROPHY :—

ATROPHY of the mucous membrane of the intestine may occur in any wasting disease, such as tuberculosis, cancer, etc., or as a result of chronic inflammatory conditions, and is frequently seen in cases of pernicious anæmia and in children the subject of marasmus. Atrophy of the various coats may occur from interference with function, and is sometimes seen as a result of starvation, or in the intestine below the site of a stricture, or even throughout the whole of the intestine in cases of cancer of the œsophagus or of the cardiac or pyloric orifices of the stomach. The atrophy is sometimes masked by a general œdematous condition of the intestinal mucous membrane.

HYPERTROPHY, especially of the muscular coat, occurs above the sites of strictures or in cases of chronic obstruction produced by other causes, and is usually associated with **dilatation.** Congenital hypertrophies of the various sphincteric areas of the alimentary canal are described on pp. 747, 755.

Hypertrophy of the lymphoid tissue is a very marked and constant feature in those cases which have been described under the term **"lymphatism,"** the solitary follicles standing out as little bead-like swellings, and the Peyer's patches often shewing even more marked swelling than that seen in typhoid fever before ulceration.

DEGENERATIONS :—

The most important of these is **amyloid** or **waxy degeneration**, which is usually associated with waxy changes in the liver, kidneys, and spleen, in tuberculous disease or in syphilis. It affects the arteries and capillaries of the mucosa and submucosa, and is seen especially in the vessels of the villi. The intestine looks smooth and pale or greyish in colour, but the condition is best detected by the application of iodine, when the vessels shew as a mahogany-brown network. This degeneration is usually associated with chronic catarrh. Superficial erosions or ulcers may be present.

CIRCULATORY DISTURBANCES :—

(a) **CHRONIC VENOUS CONGESTION** is a common pathological change in the intestine, and is the result of obstruction to the portal circulation or of a general venous obstruction. Diseases of the liver—especially cirrhosis—and diseases of the heart and of the lungs, are the most prominent factors in its causation. The mucous membrane becomes swollen, and assumes a dark bluish or even a slate-grey colour. Hæmo-

rrhages in the submucous and mucous coats are frequently seen. There usually is associated catarrh, and, perhaps, œdema, the latter condition being, as a rule, specially marked in the duodenum and upper part of the jejunum.

(b) **HÆMORRHAGE.**—Petechial hæmorrhages occur in the mucous and submucous coats of the intestine in various infective diseases, in cases of profound anæmia, in poisoning with phosphorus and other substances, and in chronic venous congestion. Larger hæmorrhages may occur from any part of the intestinal tract after severe burns of the skin, or of the skin and subcutaneous tissues: secondary to malignant growths, and as the result of intense inflammatory changes in the intestine itself, especially in cases of specific infection and where ulceration occurs, as in typhoid fever, in dysentery, in ankylostomiasis, and in duodenal ulcer. Large hæmorrhages either into the lumen or into the wall of the intestine occur in **Henoch's purpura,** and may simulate intussusception with acute obstruction, giving palpable sausage-shaped tumours. They may be followed by acute inflammatory changes, necrosis, gangrene, ulceration, peritonitis, etc., and are often fatal. Obstruction of the superior mesenteric artery or some of its branches is a comparatively rare condition, but when it occurs, as by embolism or thrombosis, great engorgement follows, often with hæmorrhage, the area of infarction usually undergoing necrosis and gangrene before any collateral circulation is set up. Strangulation, or intussusception, however produced, may give rise to hæmorrhage. Clinically, such conditions are characterised by the passage of blood in the stools. The amount and appearance of such blood vary greatly according to the site and nature of the lesion. It may be clotted or fluid, bright red if fresh, or—if altered by the action of the sulphuretted hydrogen in the bowel—of a brownish-black or black colour, the condition being then known as **melæna.** It may be so small in amount as to be diagnosed only by special tests for "occult blood." Blood in the stools may, of course, also originate from some lesion such as malignant disease or simple ulcer of the stomach, or the blood may have been swallowed.

Local hæmorrhage from the rectum itself may result from the rupture or ulceration of **hæmorrhoids,** which are produced by varicose dilatation of the veins of the rectum and anal canal. They are found usually at the lower part of the bowel, **outside** or **inside** the sphincter ani. The main cause of their production is obstruction of the portal venous circulation, which may be brought about by such conditions as cirrhosis of the liver, repeated pregnancies, tumours in the pelvis, or chronic constipation; but another important factor is obstruction to the systemic venous circulation. The hæmorrhoidal veins—being radicles of the portal vein, and also communicating freely with the neighbouring tributaries of the inferior vena cava—become dilated when there is interference with the blood-flow in either of these great systems. In chronic constipation, the fæces become unduly solid, and cause constant pressure

on the ascending veins, the contraction of the rectal wall is increased in force, and this tends to constrict the apertures through which the veins pass, and the expulsive expiratory efforts, which raise the blood-pressure in the portal and systemic venous system, are prolonged. The repeated and severe distension thus induced leads to the production of permanent varicosity.

The **hæmorrhoids** may be external and the veins surrounding the anal margin be alone distended; but, more commonly, **internal** and **external** piles occur together. Usually, the connective tissue supporting the veins is hypertrophied as a result of repeated irritation or recurrent inflammatory attacks.

Internal hæmorrhoids consist primarily of a dilatation of the radicles of the superior hæmorrhoidal vein and, secondly, of connective-tissue increase in the columns of *Morgagni*. At first. they may appear as flat, longitudinal folds of mucous membrane, but, later, they increase in size, and become more rounded and even pedunculated. The distended veins may rupture, or ulceration may take place. As they increase in size, they may become **prolapsed** through the anus. The hæmorrhoids appear as polypoid elevations of a dark red, congested appearance. **On section,** these are found to consist of dilated veins, with more or less inflammatory connective tissue as a supporting structure. Thrombosis may occur in them; the clot may organise and the pile be reduced to a small fibrous mass; or an infective phlebitis may be set up.

INFLAMMATION :—

The inflammatory affections of the intestine involve especially the mucous and submucous coats, and vary, both in character and in intensity, from those which shew merely catarrhal changes to those in which there is suppuration or extensive ulceration.

(1) **ACUTE CATARRHAL ENTERITIS** is a very common affection of children, but may occur, especially in the duodenum, in adults. The causal factor is usually the ingestion of unsuitable food, or exposure to cold; or the condition may occur as the result of one of the acute infective fevers. In some of the severer affections of the bowel, *e. g.* in the summer- or autumn-diarrhœa of children, there seems little doubt that bacteria, in most cases in contaminated milk and other foods, play an important part. The large intestine, with the cæcum and the vermiform appendix, are common sites, but the condition frequently occurs at the lower part of the ileum, just above the ileo-cæcal valve, and may also be found in other parts of the small intestine. The congestion may be diffuse, or it may be localised especially to the *valvulæ conniventes* and the tissues round the solitary glands. The mucous membrane may, in addition, be swollen, soft, and covered wholly, or in parts, with a layer of viscid mucus. In some cases, *e. g.* in the catarrh seen in scarlet fever, measles, diphtheria, etc., there is considerable swelling of the solitary

glands, especially towards the lower part of the small intestine; whilst, in other cases, small follicular ulcers, from one-sixth to one-eighth of an inch in diameter, are seen in these swollen glands. These ulcers may heal and leave small scars.

(2) **CHRONIC CATARRH** is commonest in the large intestine, and is manifested by thickening of the mucous membrane, and proliferative changes in the glandular elements, which may lead to the formation of definite polypoid elevations. Ulceration may follow, and, in the later stages, atrophy occurs, involving, not only the mucous membrane, but also the muscular coat. The mucous membrane may exhibit marked pigmentation.

(3) **CŒLIAC DISEASE.**—Gee, in 1888, described a wasting disease of children in which there was abdominal distension without any apparent pathological lesion. This has since been described under various names by different observers, and has been more fully dealt with by Hutchison under the term **cœliac disease.** Mental symptoms of various kinds are exhibited by the patients, and, later, there may be weakness of the legs. The only *post-mortem* finding of importance is thinning and atrophy of the intestine wall. The fæces are pale and offensive and always contain a considerable excess of fat. Various hypotheses, such as deficient secretion of bile by the liver, imperfect action of the pancreas, or, that the condition is merely a chronic intestinal catarrh due to some specific type of micro-organism, have been formulated. Certainly, in some of the cases, there is a considerable excess of gram-positive organisms in the stools, but no specific causal organism has been isolated. The character of the motions suggests that the condition is a chronic intestinal catarrh, with, possibly, some pancreatic insufficiency.

(4) **FOLLICULAR ULCERATION.**—As already stated, this condition may occur in acute or in chronic catarrh. In waxy disease of the intestine and in chronic nephritis, it is commonly present. It may be found as a sequel of acute fevers, or be due to the direct action of specific bacteria on the bowel, as in typhoid fever and in bacillary dysentery. So-called **stercoral ulceration** is frequently seen in the large intestine, and especially in the cæcum, where it may become chronic; and, in many cases, it seems to be due to chronic irritation behind a stricture of the large intestine, or to the irritation caused by an accumulation of fæces. The ulcers may be solitary and somewhat isolated, but, when very numerous, the mucous membrane presents a "worm-eaten" appearance from confluence of the individual ulcers. Perforation and consequent peritonitis may occur. Ulceration, **following gastro-enterostomy,** is sometimes found at the site of anastomosis, or in the jejunum a short distance from the opening. The hyperacidity of the stomach-contents was supposed to be the main factor in producing these ulcers, but it has been shown experimentally by Wilkie that other factors are concerned, such as obstruction at the orifice, hæmatoma, the irritation of unabsorbed sutures, and the passage of solid food over the raw surface during the

healing process. The ulcers are usually small and somewhat resemble the simple peptic ulcers.

(5) **CROUPOUS** or **FIBRINOUS ENTERITIS** is a rare condition, which results especially from the action of irritant poisons, or of scybala or foreign bodies which have accumulated in the intestine. The fibrinous deposit may be in the form of irregular patches on the *valvulæ conniventes*, or it may extend more widely. The condition occurs mainly in the cæcum and other parts of the large intestine.

(6) **MEMBRANOUS ENTERITIS** is characterised by the formation of. a greyish membrane on the surface of the large intestine. It generally occurs in periodic attacks, and is commoner in women than in men. Complete or incomplete " casts " of the bowel may be passed *per anum*, these casts being composed of altered mucus, mixed with degenerated epithelial cells. Membranous enteritis, caused by *B. diphtheriæ*, has been described.

(7) **SUPPURATIVE** or **PHLEGMONOUS ENTERITIS** is sometimes seen in cases of ulcerative endocarditis and in Bright's disease. Small abscesses may form in the mucous or submucous tissue, or there may be a diffuse suppurative condition in these coats.

(8) **DUODENITIS** usually results from an extension of catarrh of the stomach. The catarrh may spread into the common bile-duct, and may, from the swelling of the mucous membrane, give rise to obstruction, with resulting jaundice. In other instances, the duodenal inflammation may be secondary to some pathological condition of the liver and bile-ducts, or to the excretion of irritant substances in the bile.

(9) **DUODENAL ULCER.**—Ulcers, resembling those occurring in the stomach, and probably caused in a similar way, are frequently found in the duodenum. **Acute ulcers** are found in acute infective diseases, and it is said that a close association exists between duodenal ulcer and appendicitis, and that the appendix is frequently the source of the infection. Burns are said to be causal of duodenal ulcer. We have never seen any evidence of this in the *post-mortem* room.

Chronic Ulcers, presenting the characters of the simple peptic ulcers of the stomach, are found usually within an inch of the pylorus, and are generally situated on the upper and anterior wall. Hæmorrhage is frequent, and particularly from ulcers found on the posterior wall. Perforation may occur. Shallow developmental depressions are sometimes seen and are apt to be mistaken for ulcers.

(10) **TYPHLITIS** and **PERITYPHLITIS** are inflammatory conditions in and around the cæcum, and should be distinguished from appendicitis. The inflammatory reaction in the cæcum may be due to the accumulation of fæcal matter, to the presence of parasites, e. g. *Trichocephalus trichiuris* (*T. dispar*), or to intense catarrh arising from other causes. Ulceration may be produced, and the ulcers may perforate and give rise to acute inflammatory conditions with **abscess-formation** outside the cæcum (peri-

typhlitis). The vermiform appendix may, in such cases, be quite healthy. Acute tuberculous ulceration in the cæcum is by no means uncommon, especially in children and young adults.

(11) **APPENDICITIS** is frequently primary, but also results from an extension of inflammation from the cæcum. The swelling of the mucous membrane at the mouth of the appendix causes obstruction, and the secretions of the appendix are retained, rendering the mucous membrane less resistant, and allowing bacterial infection to take place more readily. In many cases, fæcal and other concretions are found in the appendix, and, rarely, foreign bodies such as grape-seeds, cherry-stones, or fish-bones. These concretions cause obstruction and irritation, and possibly inflammatory reaction, and, by some authors, are regarded as the important causal condition. In some cases, it seems more probable that these concretions, composed as they are of inspissated mucus and desquamated epithelial cells, mixed with the contents of the appendix, are formed *during the progress* of the inflammatory process. Such concretions are frequently found without any sign of appendicitis. Parasitic worms, especially threadworms, and more rarely *Trichocephalus trichiuris*, are found in the appendix. They may give rise to appendicitis, but, in other instances, no inflammatory reaction is set up by them.

Morbid Anatomy.—In the **catarrhal form** of appendicitis, there may be only slight swelling and erosion of the mucosa, with some congestion of the muscular coat and of the peritoneum. In the **necrotic** or **gangrenous form,** the mucous membrane is rapidly destroyed, the muscular wall is extensively invaded by inflammatory products, and, in certain cases, the whole of the coats are found in a sloughing condition. **Peritonitis** is an early sequel, either as a result of penetration of bacteria through the walls, or in consequence of perforation. General peritonitis or, in some cases, a suppurative condition round the appendix may follow. Between these two forms of appendicitis—catarrhal and gangrenous—there are various grades in intensity of the inflammatory process. In old-standing cases, partial, or even, in some instances, complete, obliteration of the lumen, usually commencing at the tip, and fibrosis, supervene.

(12) **SPECIFIC INFLAMMATIONS OF THE INTESTINES.**—These, though in many respects similar to the forms above described, have certain distinctive characteristics, and are caused by known, specific, bacterial, or other parasites.

(a) **DYSENTERY.**—This term has been, in recent years, more or less indiscriminately applied to any condition producing blood and mucus in the stools, or even to diarrhœa alone, but we here confine it to the two distinct forms, that due to the *Entamœba histolytica* and that caused by the bacillus of Flexner or Shiga. In this restricted sense, dysentery is mainly a tropical or subtropical disease, but sporadic cases may occur in any part of the world, and evidence has been brought forward to shew that not only " carriers " of the disease but definite cases,

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with all the symptoms, are found among people who have never been out of the British Isles. Possibly some of the cases should be regarded as having been recently infected from " carriers " or from actual cases which have taken their origin in known " dysentery areas " abroad, and not as evidence of the disease being endemic in the British Isles (see p. 355).

Ætiology.—Two distinct varieties of dysentery are distinguished—one the **amœbic,** caused by *Entamœba histolytica* (see p. 354): the other due to *B. dysenteriæ*. That due to *Entamœba histolytica* has a tendency to chronicity, and to the occurrence of relapses. In the **bacillary** form of the disease, bacteria of different types have been described. Morphologically, they all resemble the coli-typhoid bacilli, but differ in their biological characters. They affect specifically the colon, in its descending and sigmoid regions, to a greater extent than the cæcum and ascending colon. Organisms of different kinds may cause the painful passage of blood-stained stools with mucous shreds, but it is generally found that, where this condition occurs epidemically, or even in some sporadic cases, the cause is either the *Entamœba histolytica* or one of the types of *B. dysenteriæ*.

AMŒBIC DYSENTERY.—The presence of the *Entamœba histolytica* in relation to this disease is so striking that no doubt can now be entertained as to its causal relationship, but, as Dobell says, it is a " pathogenic parasite in a restricted sense. It is always a destroyer of tissue, but by no means always productive of disease. The usual type of human infection is that exemplified by the carrier of the parasite." And again, " every healthy carrier has the lining of his bowel more or less ulcerated; though the ulceration may be, and often is, superficial and almost invisible **post mortem** to the naked eye. But even quite extensive ulceration may exist without any dysenteric symptoms being evident." The disease is conveyed probably by water or food contaminated by infected fæces.

The amœboid form of the parasite dies soon after leaving the body in the fæces, and does not take part in propagating the disease. Even if it were to reach the stomach alive, which is very unlikely, it would probably be destroyed by the gastric juice. The small resistant encysted forms, however, pass unharmed through the stomach into the intestine, and become actively amœboid in the lower bowel, and make their way into the mucosa and submucous coat, upon which they feed, and in which they have their habitat. Here, in ordinary circumstances, e.g. in the carrier, they set up only a minor degree of irritation. In cases, however, in which they produce active disease, they bring about considerable, or, it may be, very marked, irritation and local destruction of the tissues. They penetrate into the lymph-spaces and into the veins, and it is probably by way of the veins, radicles of the portal vein, that they reach the liver. The lesions show a great variety of appearances depending on the stage

and intensity of the infection, but are confined to the large intestine, and are usually described as being specially found in the **cæcum** and **ascending colon.** Recent work on the subject seems to indicate, however, that the lesions may occur in any part of the large intestine, and some observers have found the sigmoid colon frequently involved and, occasionally, the rectum. The earliest lesions are in the form of small **nodules,** from the size of a pin's head to that of a pea, projecting above the level of the gut and shewing a central, yellowish area of necrosis, covered with intact mucous membrane, or with the mucosa ulcerated at the apex of the nodules. As a result of this necrosis, round or oval **ulcers,** with raised undermined edges, and containing a lemon-yellow gelatinous débris, are produced.

The *Entamœba histolytica* may be found in the submucous tissue at the margins both of the small nodules and of the ulcers. The submucous tissue may shew a serous exudate, hæmorrhage and fibrin-formation, and the exudate may extend to the muscular coat. Slight infiltrations of lymphocytes and so-called plasma-cells are also present in most cases. At later stages of the disease, **larger nodules,** 0·1 to 0·5 cm. in diameter, are found, and these may still be covered by intact and congested mucous membrane, or the membrane may be ulcerated, and the edges of the ulcer thickened. Thus is produced a pit in the mucous membrane, with thickened edges and containing greyish, gelatinous débris at its base and under its margin—the "*bouton de chemise*" ulcers. This débris is composed largely of degenerated and dead tissue-cells, but some inflammatory cells and fibrin may also be present. The neighbouring submucous tissue shews œdematous, and often hæmorrhagic, infiltration, and this infiltration may extend into the surrounding mucous membrane and the adjacent muscular tissue, the muscle-cells being swollen and their nuclei shewing chromatolysis. Lymphocytes and so-called plasma-cells are found in considerable numbers, especially round the vessels and in the tissues immediately external to the mucous membrane. Dilatation of the veins in the neighbourhood is often a marked feature, and this may be seen, on opening the abdomen, in the subserous veins of the intestine and in those of the mesentery of the colon. There is usually an extension of the ulceration, either by enlargement of single ulcers, or by the confluence of many. In this way, **ulcers** may be produced which encircle the whole gut, or there may be an **irregular ulcerated surface** involving almost the whole of the cæcum and ascending colon, with islets of intact mucous membrane, or with a honeycombed base and an extremely ragged surface—the projections representing portions in the surviving, or partially necrotic, mucous membrane which formerly separated the ulcers from one another —the involvement of the submucous tissue being much more extensive than that of the mucosa. In some cases, the surfaces of the ulcers may become covered by a dirty, greenish membrane composed of necrosed

tissue-cells, fibrin, and more or less altered blood (diphtheritic type), a condition which is, however, more characteristic of bacillary dysentery. Occasionally, the necrotic changes may be so intense as to involve extensively the muscular coat, and bring about perforation either intra- or extra-peritoneally.

The *Entamœba histolytica*, as already noted, may be found in large numbers in the fæces, in the submucous coat at the periphery of the ulcers: as well as in the submucous tissue, in the lymphatic spaces, and in the veins at some distance from the ulcerated area. They may be found in the dilated subserous veins as well as in the portal veins.

The **lymphatic glands** draining the ulcerated areas may shew some enlargement, but this is never a very marked feature. In the **liver,** the most important secondary lesion is the presence of one or more **amœbic abscesses** (p. 802); but cloudy swelling and fatty degeneration of the liver-cells are common; and, frequently, there is infiltration of the portal spaces with small round cells (lymphocytes and plasma-cells). No other characteristic lesions are found, though, in some cases, and especially those in which bacterial infection is present, pathological changes such as acute congestion of the spleen, degenerative and inflammatory changes in the kidney, broncho-pneumonia, fatty degeneration of the heart-muscle, hæmorrhages into various organs, etc., are found. These are bacterial or toxic in their origin, and may be found in any disease of an analogous ætiology.

BACILLARY DYSENTERY.—This form of the disease is caused by certain bacilli of the colon-typhoid group, especially those described by Shiga and by Flexner. Other causal organisms have been described by Kruse—these being probably identical with the Shiga type—by Strong and by Hiss and Russell (the Y-Bacillus), this latter being closely allied to, if not identical with, the Flexner organism.

Shiga's bacillus is now generally regarded as the specific microbe of the acute epidemic form of dysentery commonest in subtropical and temperate climates. The pathological condition produced is an acute, diffuse, ulcerative inflammation in the large intestine—more marked in the **descending** and **sigmoid** colon than in other regions.

There is abundant evidence that the **bacillary** form may be associated with the **amœbic** in the same patient. From a careful review of the recent literature, there seems to be very little doubt that the amœbic form has a wider distribution in the intestine than the bacillary form; and, further, that some of the large ulcerated areas which have been found in the descending and sigmoid colon, in cases where the *Entamœba histolytica* was present in the fæces, have not been proved to be caused by that amœba, but are more likely to have been " bacillary " ulcers, in cases where the infection has been both amœbic and bacillary.

In rapidly fatal cases of uncomplicated bacillary dysentery, the mucous membrane of the intestine is swollen, intensely congested and

hæmorrhagic, and the rugæ are prominent, and covered with viscid, blood-stained mucus. In cases in which death occurs somewhat later, the mucosa is necrotic, greyish and with a membranous exudate (**diphtheritic type**), and often associated with deep necrosis in the form of dirty-brown or blackish (blood-stained) sloughs (**gangrenous type**). The submucosa shews infiltration with inflammatory cells and serous exudate. At a still later stage, large ulcers are found, with undermined edges, tending to be annular, and extending down to the muscular layer. In extreme cases, the whole of the glandular tissue in the affected area may. be destroyed, the mucous coat disappearing completely, and the submucous coat shewing extensive sloughing and infiltration by inflammatory cells, fibrin, and blood. The cells are largely of the mononucleated type, and are seen collected in special foci round the blood-vessels. There are no characteristic secondary lesions in cases of bacillary dysentery, but changes similar to those found in any infective or toxic disease may be present in various organs and tissues— e. g. arthritis has been described as occurring in the larger joints.

Results.—In some cases, if the attack has been slight, and the ulceration only superficial, there may be a complete restoration of the mucous membrane. Usually, however, when healing takes place, cicatrices are left, which are generally darkly pigmented, and may give rise to contraction and to stricture of the colon. As a result of the stricture, dilatation of the intestine above the diseased portion may take place, and a secondary follicular ulceration, which is quite independent of the dysenteric infection, may follow. In other instances, the healing may be so complete, that the evidence of former ulceration is rendered apparent only by the presence of thin translucent areas in the wall of the bowel.

Asylum-Dysentery.— There is general agreement·that the causal organism of this form of ulcerative colitis is one of the *colon-typhoid* group of bacilli. From some cases *B. dysenteriæ* has been isolated, and, in most of these, it has been of the Flexner type.

A certain proportion of cases of so-called **sporadic dysentery** may be due to *B. dysenteriæ*, but many are undoubtedly caused by other organisms, e. g. *B. paratyphosus, Morgan's Bacillus,* etc. Thus, the dysenteric symptoms, which are not uncommon in children in **summer-diarrhœa,** may be due to Morgan's Bacillus or to other members of the colon-typhoid group, and probably also, in some cases, to bacteria of other groups; such cases are, therefore, not in any way related to true dysentery.

(*b*) **CHOLERA.**—In this disease, of which the causal agent is the **cholera-vibrio** or the **comma-bacillus** of Koch, the mucous membrane of the intestine becomes swollen and markedly congested, especially in the region above the ileo-cæcal valve. The superficial mucosa undergoes necrosis, and in the exposed surface, in the crypts of Lieberkühn and between the lining cells, the *spirilla* are found. The lymphoid follicles may also shew swelling and congestion. Small hæmorrhages may be

present, and the outer surface of the intestine has a rosy red, injected appearance. The lumen of the bowel contains a quantity of watery fluid, in which float ragged, whitish flakes, consisting of mucus, epithelial débris, and bacteria—these constituting the characteristic " rice-water stools," in which the organisms may be found in practically " pure culture." The blood is sometimes viscid in consistence on account of the constant diarrhœa and the consequent great drying-up of all the tissues.

(c) **TYPHOID FEVER.**--The *B. typhosus*, which is causal of this disease, is present in the intestinal contents, in the adenoid follicles of the intestine, in the lymphatic glands, in the liver, in the kidney, and .

Fig. 348.—Intestine from a case of typhoid fever, duration about three weeks, shewing swelling of a Peyer's patch with ulceration.   × 16.

in the spleen, being generally seen, in sections of these tissues, in small clumps or masses. It can usually be found in the blood in the earlier stages of the disease and may be found in the urine and in the gall-bladder. In the urine and in the gall-bladder, the organism may persist for a very long time, the infected individual thus being a " carrier " of the disease—the bacilli sometimes are discharged for several, and, in some cases, for many, years in the urine and in the fæces. Examination of the blood in the early stage of the disease is important in diagnosis, as the organism may be demonstrated in culture before the agglutinins have developed in sufficient quantity to give an agglutination-reaction.

Pathological Anatomy.--The main seats of the lesion are the **adenoid structures of the lower part of the small intestine**—the Peyer's and the solitary glands—the **mesenteric glands**, and the **spleen**. During the

first week of the disease, the solitary glands and the Peyer's patches become swollen and inflamed, are markedly raised above the surface of the intestinal mucous membrane, and may be pale or somewhat reddish in colour. The solitary lymphoid glands in the large intestine may also be swollen. The initial **swelling** in some of the glands seems to subside; whilst in others it increases in amount, and the gland becomes firmer and paler (*see* fig. 349). Small areas of **necrosis** appear in the swollen part, and these, increasing in size, coalesce with one another and so form irregular **sloughs**, which are usually bile-stained. Towards the end of the third week, the sloughs become separated, and irregular

Fig. 349.—Intestine from an early case of typhoid fever, shewing great swelling of a Peyer's patch. ×15.

ulcers are formed (figs. 348 and 350). The ulcers are usually oval, their long axis being parallel with that of the intestine. The floor may be irregular, if the sloughs have not completely separated, but it may be smooth and be formed by the muscular wall. The edges of the ulcers are undermined. If the ulcerative process does not penetrate deeper, the peritoneal coat shews very slight alteration. The necrotic changes may, however, spread through the muscular and peritoneal coats, and a **perforation**—usually of small size—with escape of fæcal contents into the peritoneal sac and resulting general **peritonitis**, may occur. On **microscopical examination**, the swelling of the Peyer's and solitary glands is seen to be due largely to a proliferation of the endothelial cells of the lymphatic and capillary vessels, and those of the adenoid network. These endothelial cells are actively phagocytic, and some of

(b)   (a)

FIG. 350.—Portions of the small Intestine from cases of typhoid fever of about
three weeks' duration.

(a) Lower end of Ileum and Ileo-cæcal junction, shewing great swelling of the Peyer's
patches and solitary glands, preceding ulceration. (Edinburgh University Anatomical
Museum. Catalogue No., Al. E. g. 9.)

(b) Pieces of small Intestine shewing the early stages in the formation of ulcers. The
upper piece shews a small slough in a swollen Peyer's patch. The middle portion shews
the separation of two sloughs in a similar patch. The lowest piece shews a small ulcer
forming in a swollen solitary gland. (Edinburgh University Anatomical Museum. Cata-
logue No., Al. E. g. 6.) [1]

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[1] Drawings from these preparations appeared in Lancereaux's *Atlas of Patho-
logical Anatomy* (English Translation by Greenfield), plate lxix.

them may fuse, forming giant-cells which retain their phagocytic properties. When recovery takes place, the ulcer cicatrises. The cicatrix is, often, pigmented, and may remain permanently as a flat area in which the intestinal wall is thin and transparent. The destroyed lymphoid tissue may not be restored.

The **mesenteric glands** corresponding to the infected area become swollen and softened, and small areas of necrosis (**focal necrosis**) are seen in them. The **spleen** is enlarged, usually somewhat firm, and of a dark
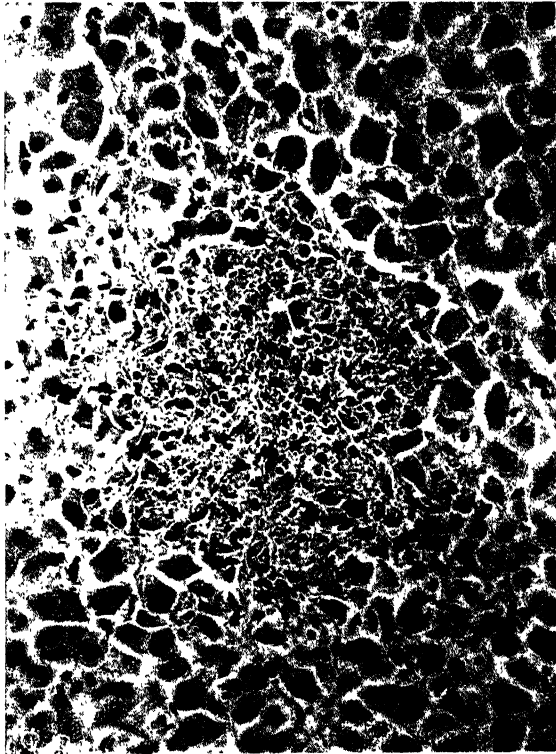
FIG. 351.—*Liver.* Shewing an area of focal necrosis, in a case of typhoid fever. × 300.

red colour, and, on microscopical examination, is found to contain small clumps of the bacilli. The **liver,** and, more rarely, the **kidneys,** may shew areas of **focal necrosis,** whilst cloudy swelling and fatty changes are almost constant features. **Acute nephritis, bronchitis, broncho-pneumonia, ulceration in the larynx, Zenker's degeneration of muscle, necrosis,** and **abscess-formation in bones**—especially in the ribs and the tibiæ—**arthritis, phlebitis, meningitis,** etc., may occur as complications.

(*d*) **PARATYPHOID FEVER.**—The clinical picture of this disease conforms so closely to that of **typhoid fever** that the diagnosis between

the two must be based mainly on bacteriological findings and agglutina-
tion-reactions. The causal organisms are of the colon-typhoid group
and conform to two definite types distinguished as *B. paratyphosus A.*
and *B. paratyphosus B.* The mortality of this disease is low, and the
description of the morbid anatomy given here is based on comparatively
few cases.

Small Intestine.—In the majority of the cases, there is ulceration of
the small intestine, the ulcers resembling those of typhoid fever and
occurring mainly in the Peyer's patches and solitary glands. They may
be widely scattered throughout the ileum, but are usually confined to
the lower two feet, and the region of the ileo-cæcal valve shews the most
marked affection. In some recorded cases, the Peyer's patches have been
swollen but not ulcerated, and, in others, no obvious lesion was present
in the small intestine, though there was extensive ulceration in the cæcum. ·

Large Intestine.—This is much more frequently affected than it is in
typhoid fever. The lymphoid follicles may be swollen, hyperæmic and
ulcerated; and, in severe cases, there may be extensive ulceration, especi-
ally in the cæcum, and this ulceration sometimes spreads along the colon
for a varying distance. Ernest Glynn has reported a case of infection by
B. paratyphosus B., in which the " mucosa of the transverse and descending
colon was swollen, dark red, and covered with minute ulcers; no sloughs
could be seen; the extravasation of blood had extended under the peri-
toneum and between the layers of the mesentery." There were ulcers
in the Peyer's patches, and also in the ascending colon and rectum.

Perforation of the ulcers, both in the large and in the small intestine,
may occur, giving rise to **peritonitis.**

An ulcerated, gangrenous and perforated **appendix** has been found in
a few cases, but always associated with ulceration in other parts of the
intestine. Other lesions, such as inflammatory and suppurative changes
in the **gall-bladder,** abscesses in the **liver,** and **broncho-pneumonia** and
gangrenous pneumonia, may be found, but are not characteristic. **Par-
otitis, lymphadenitis** of the neck, **otitis, kidney-** and **brain-abscesses,
laryngeal ulcerations, meningitis, arthritis,** etc., have been observed, and
B. paratyphosus B. isolated from some of these conditions. There are
no striking differences in the *post-mortem* appearances between the lesions
caused by the two types of the bacillus.

Like *B. typhosus*, both types of the organism occur in the fæces and
in the urine, and may be isolated from the blood in the early stages of
the disease. *B. paratyphosus A.* can be distinguished from *B. para-
typhosus B.* by its agglutination-reactions.

(e) **TUBERCULOSIS OF THE INTESTINES** is specially associated
with pulmonary tuberculosis, but it may occur as a **primary** affection of
the intestine, especially in young children. The cause of infection is
the swallowing of tuberculous sputum, or the ingestion of milk or other
food containing *B. tuberculosis.* The principal seat of infection is the lower

part of the ileum, the Peyer's and the solitary glands becoming swollen, either uniformly, or in scattered, irregular areas, and tuberculous foci also frequently occurring in other parts of the submucous or mucous coats. These swollen patches, covered, at first, by the mucous membrane, which may shew a catarrhal condition, later, undergo a central caseous necrosis, and over them the mucous membrane sloughs, forming small ulcers, at first rounded, but soon, by coalescence, spreading and becoming very irregular. Both the floor and the edges of the ulcers are infiltrated and thickened, the floor appearing caseous, ragged, and granular, and the margin raised and irregular. The ulceration spreads peripherally, and also more deeply, into the bowel-wall, and, at its lateral edge, it may extend transversely in the intestinal mucosa beyond the margins of the Peyer's gland or solitary lymphoid follicle, if it has either of these as its site of origin, as is commonly the case; and it may, ultimately, almost, or even completely, encircle the bowel. In its further spread, it extends to the muscular and peritoneal coats, and produces, in the deeper parts of the serous coat, a number of tubercle-granulations (fig. 353) —often seen along the lines of the lacteals or other lymphatic channels, by which the process tends especially to spread. Thickening of the serous coat and adhesions to surrounding parts are thus produced, and the situation of the ulcer in the intestine can often be detected, on opening the abdomen, by the presence on the peritoneal surface of these thickened, inflamed areas, in which whitish or greyish tubercle-granulations are studded. An over-

Fig. 352.—*Tuberculous Ulceration of the Intestine.* Showing the raised thickened edges and the irregular floors of the ulcers.

growth of fibrous tissue leads sometimes to contraction of the ulcerated area, and to stricture of the intestines. These tuberculous strictures may be multiple, and the lumen of the bowel, at the site of the strictures, may be very much reduced in diameter. On account of this thickening, perforation very seldom occurs—though it may do so in certain cases of **acute tuberculous ulceration**. In such cases, the edges are usually ragged and undermined, and the floor is not infiltrated to any marked degree—the appearance resembling typhoid, rather than typical tuberculous, ulceration. The intervening mucous membrane often shews catarrh and congestion, which may be very intense. **On microscopical examination,** the nature of the lesion is detected by the presence of tubercle-follicles, caseation, and the causal bacilli.

The **cæcum and large intestine** are less commonly affected by the tuberculous process, the ulcers, when they occur in these regions, tending to be of the acute type and to spread widely, causing large irregular areas of destruction of the mucous membrane. The **rectum** very rarely shews tuberculous ulceration, but many cases of **fistula in ano** appear to be tuberculous in origin. The **mesenteric glands** are usually enlarged, and shew tuberculous infection and caseation. In **children** especially, the glands are very frequently infected, even though there may be no obvious evidence of any lesion in the intestinal wall itself—the bacilli probably passing directly from the intestine, by way of the lymphatics, to the glands.

(a)
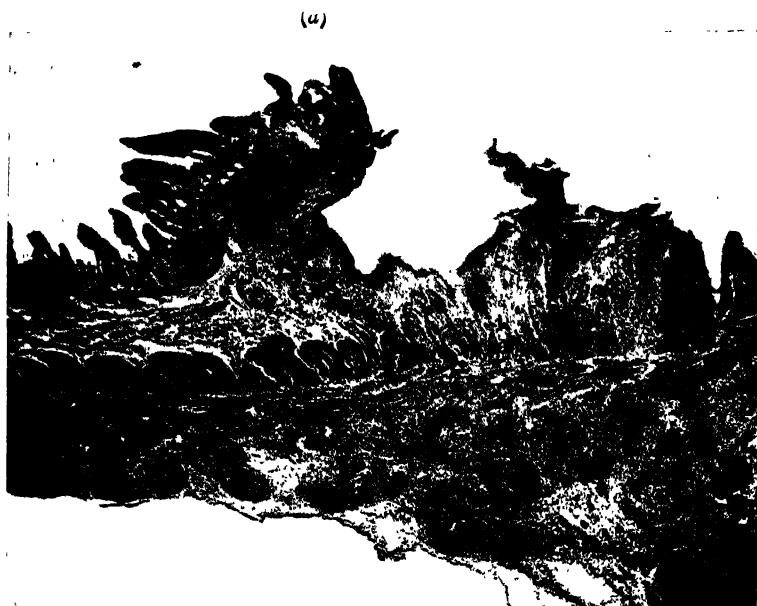
Fig. 353.—*Tuberculous Ulceration of the Intestine.* Shewing the raised, undermined edge (a): the tubercle-follicles, and especially the great thickening of the serous coat (b).   × 16.

The glandular involvement is often very considerable, giving rise to the condition of **tabes mesenterica** (*see* pp. 635–7). **Waxy degeneration** of the intestine is sometimes associated with the tuberculous condition, and is usually part of a more gereralised process, occurring especially where the lungs, bones, or joints are the seat of chronic tuberculosis. In such cases, the kidneys, liver, and spleen, as a rule, also shew the waxy change (*see* p. 60).

(f) **SYPHILIS** is a rare affection of the intestine, but gummata occasionally occur, with ulceration, cicatrisation, and stricture. Primary sores about the anus are found, especially in women.

(g) **ACTINOMYCOSIS.**—In the bowel, the cæcum and appendix are the commonest seats of actinomycosis, but the pelvic colon may be attacked. Abscesses and sinuses are formed and the parietes become infiltrated.

(h) **FIBROMATOSIS.**—In this condition, the pelvic colon and the

Fig. 354.—*Scirrhus or Hard Cancer of Intestine*, producing obstruction of humen.
(Royal College of Surgeons Museum, Edinburgh.)
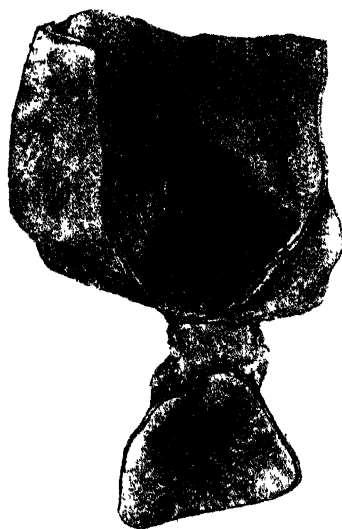
Fig. 355.—*Malignant Adenoma of the Large Intestine*, producing great narrowing—the
so-called Malignant Stricture. Note dilatation, hypertrophy, and ulceration above,
and atrophy below, the seat of stricture. (Edinburgh University Anatomical Museum.
Catalogue No., Al. E. l. 13.)

rectum may be converted into a rigid tube. The peritoneum is thickened, and, under this, is a uniform layer of dense fibro-adipose tissue; sometimes half-an-inch in thickness. The muscular layer may be atrophied, or may shew very little change; but the submucous layer is greatly thickened by an overgrowth of dense fibrous tissue. By contraction of this tissue, the mucous membrane is thrown into folds with deep recesses between them, and ulceration takes place in these recesses. No evidence of malignant disease is found, but the tissues are infiltrated with chronic inflammatory cells.

Fig. 356.—*Malignant Adenoma, Primary Growth in Large Intestine.* On the right are seen the normal mucous, submucous, and muscular coats of the bowel. On the left are the large, irregular, tube-like acini of the new growth, lined by large, dark-staining, columnar epithelium. Infiltration of the normal structures at the spreading margin is seen. × 10.

TUMOURS OF THE INTESTINE :—

Fibromata, lipomata, myomata, and myxomata may occur, and generally assume a polypoid shape. Sarcomata are not common, but both round- and spindle-celled, as well as melanotic, sarcomata have been described. Masses of lymphoid tissue, which cannot be distinguished from lympho-sarcomata, occur occasionally in cases of lymphatic leukæmia. Lymphomatous swelling, and perhaps ulceration, may be found in the lymphoid tissue, and this condition is sometimes also seen in Hodgkin's

disease. The most important tumour of the intestine, **primary cancer,** may occur in the duodenum—in which situation it frequently invades the head of the pancreas—in the rectum, the cæcum, the lower part of the pelvic colon (sigmoid flexure), and the hepatic and the splenic flexures. It is usually **adenomatous** in type (fig. 356), though sometimes the **scirrhus** form may occur. Both forms are sometimes found in the same intestine. **Colloid degeneration** may take place in either, and also a species of mucoid degeneration in the mucin-secreting cells. The growth is often . small and localised, and frequently produces a stricture (figs. 354 and 355). Ulceration of the surface of the growth frequently takes place, and perforation may occur, especially in growths in the transverse colon. Such malignant tumours may or may not become polypoidal.

Secondary cancers are rare, except as part of a generalised peritoneal spread. Infiltration of the bowel by malignant tumours of neighbouring structures is common.

PARASITES :—

Protozoal Infections.—Various protozoal parasites are found in the alimentary tract. Except in the case of *Entamœba histolytica*, the part, if any, which some of these play in the production of irritation or actual disease of the bowel is not at present established. Diarrhœa may be present in cases in which these parasites are found, yet the same parasites may occur in apparently normal fæces. Of these parasites the most important are :—

> *Entamœba histolytica*, p. 354.
> *Entamœba coli*, p. 352, and *Entamœba limax*, p. 359 (*Endolimax nana*) (intestine).
> *Trichomonas intestinalis*, p. 368 (large intestine and colon).
> *Lamblia intestinalis*, p. 369 (upper part of small intestine).

Occasionally one finds *Tetramitus mesnili, Cercomonas*, etc.

Bilharziasis or Schistosomiasis.—The ova of *Schistosoma mansoni*, the specific parasite of **Intestinal Bilharziasis** or **Schistosomiasis** (p. 395), may cause very considerable irritation of the rectum, with the production of numerous large papillomatous growths in the region of the anus, and extending well into the rectum. The thickening may resemble carcinoma, and, in some cases, apparently, carcinoma is a secondary result of the irritation. *Schistosoma hæmatobium* (*Bilharzia hæmatobia*), either alone, or in association with *S. mansoni*, is also found occasionally in the rectum.

Among other animal parasites occurring in the intestine may be mentioned *Tænia saginata* and *Tænia solium, Dibothriocephalus latus, Ascaris lumbricoides, Ankylostoma duodenale, Oxyuris vermicularis, Trichocephalus trichiuris (T. dispar), Paragonimus westermani, Heterophyes heterophyes, Balantidium coli*, etc. These are described under **Animal Parasites** (pp. 386 *et seq.*). They may give rise to enteritis with a varying degree of diarrhœa ; and mucus and blood may be found in the stools.

DISEASES OF THE PERITONEUM

CONGENITAL ABNORMALITIES.—There may be an exaggeration of the normal pouches, an abnormal shortness of the mesentery, a laxness of the various ligaments, or the persistence of processes and connections which in the ordinary course of development become obliterated. Dermoid cysts, and other cystic developments of unknown origin (air-cysts, etc.), have been described.

CIRCULATORY DISTURBANCES :—

(*a*) **ACUTE CONGESTION** (*see under* **Inflammation**).

(*b*) **CHRONIC VENOUS CONGESTION,** resulting from any of the usual causes of this condition, may shew itself in the peritoneal sac. The peritoneum becomes œdematous, and accumulation of fluid occurs. The fluid may be clear, or blood-stained from rupture of the distended vessels.

(*c*) **HÆMORRHAGES,** in the form of petechiæ, are found in various septic and hæmorrhagic diseases, and in parts adjacent to acute inflammatory foci. Minute hæmorrhages occur in cases of chronic venous congestion, and in phosphorus-poisoning, snake-bite, etc. When **recent,** the petechial hæmorrhages are bright-red in colour. At a **later period,** the remains of these are frequently seen as small, black, pigmented spots immediately under the serous surface. Larger hæmorrhages may result from traumatism, laceration of the liver, spleen, or kidneys, or from the rupture of cysts, extra-uterine pregnancies, etc. Hæmorrhage is found in infarction of the intestine, and in some cases of tuberculosis or cancer of the peritoneum.

(*d*) **ASCITES** develops as part of a general dropsy in cardiac or in renal disease; or it may be due to obstruction of the portal circulation, especially in cases of cirrhosis or cancer of the liver. Chronic peritonitis may lead to accumulation of fluid in the sac, but does not necessarily do so. The fluid is usually clear and colourless, or perhaps somewhat yellowish in colour, but it is sometimes hæmorrhagic in character. Where there has been obstruction or rupture of lymphatic channels, for example in some filarial diseases or in tuberculosis, the fluid appears milky from the presence of finely divided fat or chyle (**chylous ascites**). A fluid, somewhat resembling that of chylous ascites in its naked-eye characters, is occasionally seen in cases of cancer—where there is considerable degeneration of the cells, the admixture of the cells containing fatty particles with the fluid, giving it a milky appearance—in tuberculosis of the mesenteric glands, and also in some obscure cases in which the particles are albuminoid, not fatty.

As a result of the ascites, chronic fibrous thickening of the peritoneum is not infrequent.

INFLAMMATION, or PERITONITIS :—

Peritonitis occurs as a result of the direct spread of infection through a damaged, but not necessarily perforated, intestinal wall; or it may be secondary to appendicitis : to the escape of the contents of the stomach or of the intestine into the peritoneal sac : or to the secondary spread to the peritoneum of an inflammation—suppurative or non-suppurative—in, or round, the intestines or other abdominal organs, *e.g.* the Fallopian tubes. Direct spread through the diaphragm from the pleural cavity, and extension from septic wounds in the abdominal wall, may occur. A primary affection of the peritoneum is not so common, but may arise during the course of an attack of acute rheumatism, acute lobar pneumonia, or in Bright's disease. A primary pneumococcal peritonitis is occasionally found without any obvious pathological lesion elsewhere.

Pathological Anatomy.—In the earlier stages, there is marked hyperæmia, with serous exudation. Fibrin is formed, and this is deposited as a fine reticulum on the surface of the intestines. The coils become glued together by this exudate. The adhesions formed are at first soft, and thus the surfaces in contact are easily separated. If the condition progresses, greater numbers of leucocytes emigrate, and, in some cases, the exudate becomes purulent. The pus is found first round the original focus of infection; but, if not localised by adhesions, it gravitates to the pelvic cavity or to the right and left lumbar regions. The course, however, may be influenced by the arrangement of certain peritoneal folds. Thus, effusions resulting from perforation or inflammation of the duodenum, gall-bladder. and right lobe of the liver, will be directed towards the right kidney; and those arising in connection with the stomach, towards the spleen. Effusions in connection with the appendix tend to gravitate into the pelvic cavity or are directed upwards alongside the colon towards the right renal or sub-hepatic pouch. The endothelial cells of the peritoneum swell and multiply, and many of them are shed. A certain amount of infiltration with inflammatory products occurs in the sub-endothelial layer of the intestine, which becomes swollen and œdematous. Tympanitic distension takes place on account of paralysis of the muscular coat of the gastro-intestinal canal.

The characteristics of the various cells found in the exudate at the different stages have been fully discussed under **Inflammation** (p. 174).

If **recovery** takes place, a varying degree of adhesion between neighbouring structures, *e.g.* the adjacent coils of intestine, or between these and the abdominal wall or some of the abdominal organs, generally remains.

Localised Intra-peritoneal Suppuration.—Localised inflammation, or localised collections of pus within the peritoneal cavity, may arise from various causes. Such conditions are seen in localised appendix-abscess, round disease-foci in the female pelvic organs, as a result of slow leakage from a gastric or duodenal ulcer, in inflammatory processes around a cancerous growth of the intestine, and in disease of the gall-bladder, bile-ducts, or pancreas. "Residual" abscesses may occur in any part of the peritoneal cavity after the subsidence of a widespread peritonitis. Abscesses due to chronic tuberculosis are found in various situations.

Sub-phrenic or sub-diaphragmatic abseess may arise from almost any intra-abdominal lesion—the commonest, however, being perforation of an ulcer of the stomach or duodenum, suppurative conditions of the liver and its ducts, and appendicitis. In some cases, the focus of infection is above the diaphragm—in the lung or pleura.

CHRONIC PERITONITIS may be a sequel of an acute attack, but a slowly developing peritonitis, with the formation of fibrous adhesions, sometimes occurs in connection with Bright's disease, or in cancer of the peritoneum. Local thickenings of the capsule of the liver and of the spleen are frequently seen in diseases of these organs, and, very commonly, there are adhesions between them and the parts around. These conditions arise as a result of a proliferative over-growth of the pre-existing fibrous tissue of the part, caused by chronic irritation—for example, around a gall-bladder containing gall-stones—and should not be classed as "inflammation." Chronic peritonitis is probably most frequent in connection with the female generative organs, and often results in adhesions which may cause considerable distortion and, perhaps, displacement of the organs. It is seen as the result of syphilis, e. g. on the surface of the liver (syphilitic perihepatitis).

TUBERCULOSIS of the peritoneum is often very widely spread, and sometimes unattended by any marked acute inflammatory reaction. On the other hand, the acute inflammatory changes associated with the condition may be very intense, and the exudate be hæmorrhagic. Frequently, however, a slowly developing, subacute inflammatory reaction takes place, and this leads to extensive infiltration, and the formation of irregular, firm adhesions. The **great omentum** may be so infiltrated, thickened, and retracted, that it measures over an inch in antero-posterior diameter—forming a characteristic cake-like mass towards the upper part of the abdomen. The tuberculous nodules vary greatly in size. In the more acute forms, they are usually small—sometimes extremely minute and resembling fine grains of pepper on the peritoneal surface—but, in the chronic cases, they are comparatively large. They are greyish or yellowish and opaque, and have not the pearly lustre so often seen in secondary nodules of cancer. They are frequently pigmented.

Serous or sero-purulent exudate is sometimes present. When present, it is usually contained in irregular saccules between the adhesions. There may be a varying degree of involvement of the lymphatic glands in the tuberculous process.

Ætiology.—Tuberculosis of the peritoneum is commonest in children, but may occur at any age. The condition is usually secondary to tuberculosis of the glands or of some abdominal viscus. The commonest sources are tuberculosis of the mesenteric or retro-peritoneal glands, and of the ovaries and Fallopian tubes. Intestinal tuberculosis rarely gives rise to a general peritoneal infection—only localised patches on the outer wall of the bowel, corresponding in their position with the ulcers in its interior, being, as a rule, affected. Spread of a tuberculous infection through the diaphragm from the pleura may occur; and, in rare instances, tuberculosis of the vertebræ and tuberculosis of the appendix are sources of infection. Tuberculous peritonitis is sometimes part of a generalised acute miliary tuberculous infection.

Results of the Process.—The adhesions often give rise to serious obstruction of the intestine. In very chronic cases, calcareous deposits may be found in the adhesions and in the infected glands.

TUMOURS :—

Small pedunculated tumour-like masses—sometimes called "**lipomata**" —**and cysts** arising from the *appendices epiploicæ* are frequently seen. These are not true tumours, but merely overgrowths of the *appendices*. Multiple **fibromata** and **sarcomata** of retro-peritoneal origin occur. Primary tumours of large size, in which a plexiform arrangement of vessels exists —the so-called **Angio-sarcomata**—have been described. **Primary carcinoma** is not common, but some of the so-called **endotheliomata** (or **mesotheliomata**), which have been described as occurring in the peritoneum, seem to be of this nature, and a **primary colloid cancer** of the peritoneum is recognised.

Secondary growths of cancer are of common occurrence. Some of these arise by direct and continuous spread from colloid or other cancers of the stomach and of the intestines. True secondary or metastatic growths occur in association with cancer of the ovaries or other pelvic organs. Occasionally, wide-spread **miliary** nodules are met with. This **acute carcinomatosis** is always a secondary manifestation, and is probably due to the infective material being diffused by the fluid in the peritoneal sac, aided by the peristaltic movements of the intestine, the cancer-cells entering stomata and being carried to the sub-peritoneal tissues. The cancer-nodules are frequently flat and firm, and have a pearly lustre. They are, as a rule, specially numerous on the great omentum, and on the appendices epiploicæ, which are both highly absorbent structures. The abdominal surface of the diaphragm generally shews a great number of the cancer-nodules, and, as the lymphatics

of the diaphragm communicate freely with those of the pleura, spread to the latter structure frequently takes place.

Chylous cysts, due to obstruction and distension of the lacteals, are sometimes seen on the surface of the intestine.

PARASITES :—

Hydatid cysts are the only important animal parasites of the peritoneum.

CHAPTER XX

DISEASES OF THE LIVER

BRIEF reference must be made to some of the more salient anatomical facts in relation to the structure of the liver, as these have an important bearing upon the pathological conditions found in the organ. The fibrous capsule which lies under the serous coat is very thin and transparent, and is continuous with the delicate supporting stroma of the organ. At the portal fissure, it becomes continuous with Glisson's capsule—the fibrous tissue which ensheathes the branches of the portal vein, the hepatic artery, and the bile-ducts.

The liver-substance is composed of a multitude of polyhedral lobules, each lobule being composed of a mass of cells which appear to be more or less radially arranged about the central point of the lobule. The branches of the portal vein, the hepatic artery, and the bile-ducts, extend in the sheath derived from Glisson's capsule, to the periphery of the lobule. The branches of the portal vein (inter-lobular veins), by which most of the blood comes to the liver, send capillaries into the lobule, and these at the centre open into the central or intra-lobular vein. These intra-lobular veins unite to form larger veins, the sub-lobular, which open into the hepatic veins. Between the capillaries, lie the rows or columns of hepatic cells; and, separating these blood-channels from the liver-cells, there are at places the stellate cells of Kupffer. The function of these cells and their relation to the liver are still doubtful. The capillaries probably have a delicate wall composed of endothelial cells, but it is a matter of dispute as to whether the latter lie directly in contact with the liver-cells or are separated from them by a delicate layer of fibrous tissue. The study of the various pathological changes to which these structures are liable, leads one to believe that this connective-tissue layer must exist; but, in the normal liver, if present, it is so delicate that its presence cannot be satisfactorily demonstrated by our present methods of staining, and its existence is denied by many eminent histologists.

The larger bile-ducts are lined with columnar epithelium, and the smaller channels, with cells of a cubical type. The biliary capillaries, which are lined with delicate flattened cells, originate within the liver-lobules, and their primary tributaries seem to be formed by the hepatic cells themselves.

MALPOSITIONS and MALFORMATIONS :—

The liver may be **transposed** in cases of general transposition of the viscera (*see* fig. 341). Abnormalities in the arrangement of the lobes, and the presence of **accessory lobes** and **sulci,** are of anatomical, rather than pathological, interest. **Displacements** are frequently observed, the liver being displaced either upwards or downwards, and the **suspensory ligament** often elongated. The **hepatic artery** may be doubled; or the **ductus venosus** remain patent.

ACQUIRED DEFORMITIES and **DISPLACEMENTS,** such as those produced by the pressure of tumours or of fluid accumulations, are

common. Pressure on the lower part of the thorax, such as is brought about by tight-lacing or by prolonged wearing of a tight belt, causes a flattening of the liver, and the production of transverse grooves, especially in the right lobe. At the bottom of such grooves, the capsule is thickened, and there is considerable atrophy of the liver-tissue. These grooves may be well defined and so-called " artificial lobes " of the liver be produced, these lobes being, in extreme cases, attached to the main part of the organ by only the thickened capsule, fibrous tissue, and vessels (see fig. 357). Depressions corresponding with the lines of

Fig. 357.—Liver. Shewing Atrophic Sulci, the result of pressure.

the ribs are frequently seen. Antero-posterior atrophic sulci may occur upon the upper surface of the liver, as the result of increased intra-abdominal pressure (see fig. 357).

Perihepatitis.—This condition, which is not necessarily due to actual inflammation, is very common. The capsule is thickened in varying degree, and extensive adhesions between it and the adjacent organs or tissues are sometimes found. It results from any chronic irritative condition in the peritoneal cavity, such as the continued accumulations of ascitic fluid or of pus. It occurs to a marked degree in acquired syphilis of the liver, and is seen also in chronic enlargements of the organ, and in cases of cirrhosis. It sometimes results from healed tuberculous peritonitis.

REGENERATIVE CHANGES IN THE LIVER [1]:—

It has been shewn by experiment that, if one-half or even three-quarters of the liver of a rabbit be removed, repair takes place very

FIG. 358.—*Multilobular Cirrhosis of the Liver*, with large, projecting, comparatively smooth nodules. These latter are areas of compensatory or complementary hypertrophy.

rapidly, and that the organ may regain its ordinary size—the newly-formed tissue being, in the main, indistinguishable from liver-tissue. Mitotic figures are easily demonstrated in the newly-formed tissue, and

[1] Lindsay Milne, Thesis for Degree of M.D., University of Edinburgh, 1908; and *Brit. Med. Jour.*, October 17, 1908, p. 1169. Turnbull and Worthington, *Archives of Pathological Institute*, London Hospital, 1908, vol. ii., pp. 35 et seq. (Older references are given in both of these communications.)

there seems to be no reason to doubt that the repair takes place by a pro-liferation of liver-cells. The part played by the bile-ducts in this new formation is more uncertain, but, from the most recent work on the subject, there is a considerable amount of evidence that the cells lining the bile-ducts may be transformed at any rate in certain areas—though it may be, imperfectly—into secreting hepatic cells.

These **regenerative changes** are very common **in pathological conditions of the liver,** especially in cases in which there is any destruction, with loss of function, in the secreting cells of the organ. Thus, in **acute** and **sub-acute liver-atrophy,** in **chronic venous congestion,** in **abscess-formation,** in **cancer,** in **cirrhosis,** etc., there may be seen, microscopically, irregular areas in which the liver-cells stain somewhat intensely, shew an atypical arrangement, are irregular in size and shape, and exhibit active pro-liferative changes. Mitotic figures in the proliferating cells are often found. These are undoubtedly **regeneration-areas,** and are probably to be regarded as compensatory in nature. The new bile-ducts, which occur, apparently in excess, in some of the pathological conditions mentioned above, appear to arise by proliferation from pre-existing bile-capillaries, though some authors still hold that they arise from liver-cells. Lindsay Milne opposes both views, and is of opinion that the appearances suggesting the occurrence of proliferation of bile-ducts are really due to the flattened epithelial cells lining minute pre-existing bile-channels becoming swollen and cubical in form and thus more apparent.

CIRCULATORY DISTURBANCES :—

(a) Pale (**ANÆMIC**) patches are frequently seen on the surface or in the substance of the liver, and are the result of pressure by the ribs or by neighbouring viscera—usually after death.

(b) **ACUTE CONGESTION** occurs in various toxic and septicæmic diseases. As cloudy swelling (q.v.) supervenes, the previously congested vessels become emptied of their blood by the pressure of the swollen liver-cells.

(c) **CHRONIC VENOUS CONGESTION** results from obstruction to the circulation in the liver. The commonest cause is valvular disease of the heart, especially mitral disease; but it may also result from obstruc-tion to the pulmonary circulation, or pressure on the inferior vena cava at its upper part. There is produced a general engorgement of the venous circulation, not in the liver alone, but in other organs as well. The liver at first increases in size, becomes much firmer in consistence, and is darker in colour. On section, the hepatic veins are greatly dilated, and the dark central veins of the lobules, surrounded by lighter areas of liver-cells, may be seen. At later periods, fatty changes take place in the cells, and an irregular mottling of the surface is observed—the yellowish, fatty areas alternating with the dark-red congested parts. Yellowish or greenish bile-staining also occurs. On account of this

mottling and variegation in colour, and the resemblance to the cut surface of a nutmeg, the term **nutmeg-liver** has been applied to the condition. As the process advances, there is considerable atrophy of the liver-cells from compression between the distended vessels, and a reduction in the size of the organ takes place. The dark, congested areas, seen on section, become more pronounced—from progressive involvement of the capillaries around and opening into the central vein—hence the name **central red atrophy** applied to this stage of the disease. The capsule usually becomes thickened and wrinkled, and, frequently, has a morocco-leather

FIG. 359.—*Liver.* Chronic Venous Congestion. Section on left—early stage, shewing the large dilated hepatic veins, etc. The small dark spots are the areas of central red atrophy round the central veins. The other sections shew more advanced stages, with a greater extent of vascular dilatation, the darker areas being confluent.

appearance, resembling that seen in fine cirrhosis. The distribution of the change is often unequal, being, in many cases, most marked in the distal portions, especially of the left. lobe. Localised areas are also common, as a result of local obstruction to the hepatic veins **within** the liver, *e. g.* from the pressure of tumours, etc.

On **microscopical examination,** in the early stages (fig. 360), the central vein of the lobule is distended and its walls are thickened, the capillaries adjacent to it are also engorged, and there is consequent atrophy of some of the intervening liver-cells. Yellowish granules of blood-pigment are found in varying numbers in this region. In the later stages (fig. 361), there may be merely a narrow zone of liver-cells surviving around the portal tracts, and even these cells may shew advanced fatty changes.

The remaining part of the lobule is made up of distended capillaries, the walls of which are thickened, and between which the liver-cells have completely disappeared. Blood-pigment is usually present in considerable amount. Any increase of fibrous tissue found in the liver in cases of uncomplicated chronic venous congestion is due merely to a thickening of the walls of the venules and capillaries as a result of long-standing dilatation. In such **uncomplicated** cases, there is no overgrowth of fibrous tissue extending either from the portal tract, or from
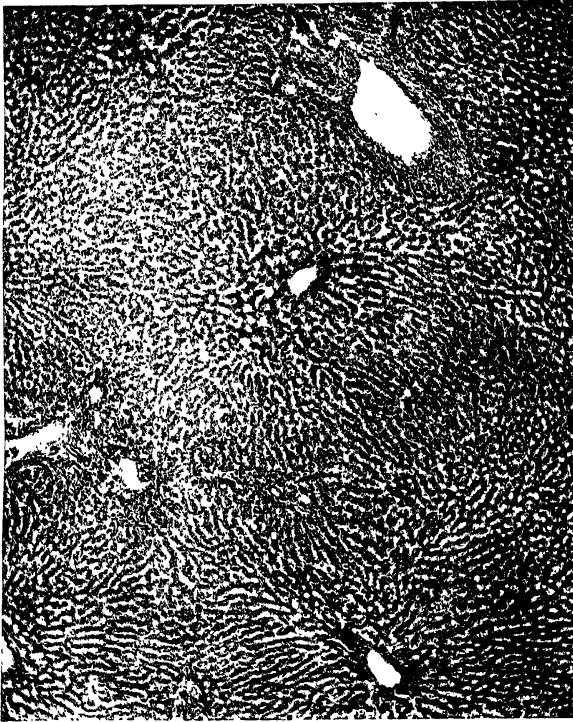
Fig. 360.—*Liver.* Early stage of Chronic Venous Congestion, shewing dilatation of centra veins and of capillaries, and deposit of blood-pigment. Note portal tract with large vein at right-hand upper corner. × 50.

the rest of the fibrous-tissue framework of the liver. **We, therefore, consider it incorrect to state that cirrhosis of the liver may be a sequel of chronic venous congestion.** Irregular areas of atypically arranged liver-cells shewing mitosis, etc., are commonly seen in advanced cases of chronic venous congestion. From the researches of Turnbull,[1] Lindsay Milne,[2] and others, there seems no doubt that these are areas of attempted restoration or regeneration of liver-tissue.

[1] Turnbull and Worthington, *Archives Path. Inst.*, London Hospital, vol. ii., 1908, pp. 35 *et seq.*

[2] Lindsay Milne, Thesis, University, Edinburgh, 1908.

(*d*) **EMBOLISM and THROMBOSIS of the PORTAL VEIN.**—Though these conditions arise as a result of pressure on, or invasion of, the vein by tumours, etc., they are usually the result of the detachment of portions of an infective thrombus, or the direct extension of this thrombus from one of the radicles of the vein—especially a mesenteric vein—in cases of septic enteritis, appendicitis, inflamed hæmorrhoids, or other infective conditions in areas from which the portal blood comes. The blocking of the vein may cause complete necrosis of the central two-thirds of the lobules, though, in some cases, comparatively little damage to the liver-tissue results—the nutrition of the cells, especially those at the periphery of the lobules, being maintained by the hepatic artery.
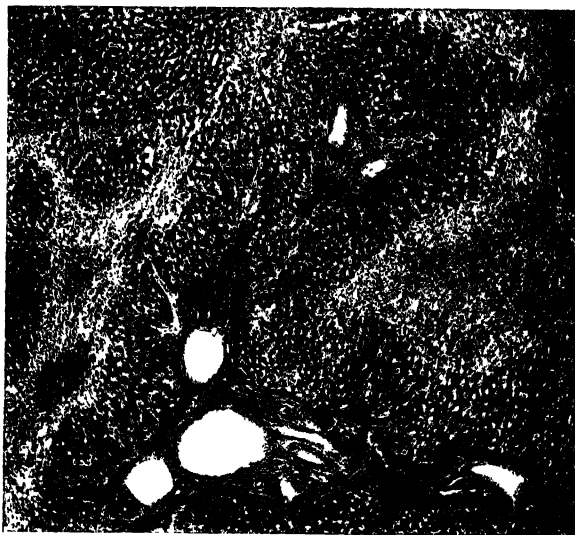
Fig. 361.—*Liver.* Chronic Venous Congestion, advanced stage, shewing atrophy of liver-cells at the centres of the lobules. Cells round the portal spaces are not involved. × 30.

If the condition becomes chronic, there is usually abundant proliferation of the connective tissue, and, perhaps, leucocyte-infiltration, of the affected portal tracts. The sepsis, however, not infrequently extends into the inter-lobular and other branches of the vein, and these may become distended and infected, with the production of large irregular suppurative areas (**pyle-phlebitis**) and considerable destruction of the liver-tissue. The obstruction of the vein sometimes brings about a dilatation of all its radicles in the abdominal viscera, and produces a condition of passive hyperæmia with ascites. If the thrombosis spreads backwards so as to involve any of the great tributaries of the portal vein, marked pathological changes may occur in the organs which they drain.

On account of the free anastomosing channels, and of the fact that the liver-tissue is nourished largely by the portal vessels, **embolism or**

thrombosis of branches of the hepatic artery usually produces little change of importance—unless the plug be of an infective nature, in which case abscess-formation may result [1]—but hæmorrhagic infarcts of the liver have been described, and, in these cases, there has usually been thrombosis in many branches both of the hepatic artery and of the portal vein, or thrombosis in the portal vein with extensive degenerative (endarteritis obliterans), and therefore obstructive, changes in the hepatic artery.

RETROGRESSIVE CHANGES IN THE LIVER :—

In studying the retrogressive processes in the liver, it must always be borne in mind that changes due to decomposition take place very rapidly in the organ. Local alterations of colour are common—a bluish-black discoloration (**pseudomelanosis**) appearing, especially where the liver is in contact with the transverse colon; and yellowish or pale **anæmic patches** shewing, as a result of the pressure of the ribs, etc. **Gas-formation** may occur after death. This is seen, in its most marked form, as an extensive honeycombing of the liver which occasionally results from infection with *B. aerogenes capsulatus*. There seems very little doubt, however, that, though the most active growth of this organism takes place after death, yet there are cases in which the emphysematous condition of the liver produced by it is of *ante-mortem* occurrence : *e. g.* in cases of gas- or emphysematous gangrene. The pseudo-cysts produced in this way are simply air- or gas-spaces without liquid contents. Their walls, formed directly of liver-tissue and without lining membrane, are dry and smooth, and the gas-producing organisms may be found in large numbers in the walls and adjacent liver-tissue.

(*a*) **ATROPHY** of the liver-cells supervenes in old age, and also in diseases which, either as a result of general toxic poisoning, or merely following interference with the absorption of food, cause general emaciation. Thus, the condition is sometimes seen to a marked degree in cases of phthisis, and in cancer of the stomach.

Local Atrophy may result from pressure by tumours in the liver, by dilated capillaries in chronic venous congestion, by dilated hepatic veins, especially if near the surface of the organ, or by the swollen capillary walls in waxy degeneration. Obstruction of the common bile-duct, by causing dilatation of its tributaries, may also bring about pressure-atrophy of the liver-cells. **Microscopically,** the liver-cells of the affected part become distorted, decreased in size, and usually pigmented. At later periods, they break down and disappear.

(*b*) **ACUTE LIVER-ATROPHY (or Acute Yellow Atrophy).** — The ætiology of this rare disease is at present unknown, but it is more or less agreed that the liver-changes are produced by some poison in the general,

[1] Lindsay Milne (*loc. cit.*) finds that experimental ligature of the portal vein in rabbits, cats, and dogs, produces rapid necrosis of the central two-thirds of the lobules; whilst ligature of the hepatic artery produces no visible effect.

or perhaps more especially in the portal, circulation. It has been sug-
gested that this poison may be produced by decomposition-processes in
the stomach or the intestine, and that it may possibly be of the nature
of a ferment which is capable of destroying the liver-cells. There seems
to be, however, much evidence in favour of the view that the condition
is an infective one.

An identical, or, at all events, very similar, pathological process has
been described in certain cases of syphilis which have died immediately
or shortly after the injection of salvarsan or its substitutes.

Acute liver-atrophy may be simulated to some degree, both clinically
and pathologically, by certain cases of septicæmia, and by cases of

Fig. 362.—*Acute Liver-Atrophy* (Acute Yellow Atrophy), shewing, at some parts, the
    entire absence of liver-cells, and, at others, degenerative changes in them. Note also
    the apparent cellular character of the portal spaces. ˙ × 30.

phosphorus- and ptomaine-poisoning; but, in studying the development
of such cases, it is obvious that there are certain essential differences
between them and true acute liver-atrophy. Thus, in cases of septicæmia,
and in phosphorus- and ptomaine-poisoning, the destruction of the
liver-cells is a sequel of acute fatty changes; whereas, in acute liver-
atrophy, the absence of fatty changes is usually—according to some
observers, with whom we agree—a very striking feature of the disease.
For this latter class of cases, where there is acute destruction or necrosis
of liver-cells without preceding fatty transformation, *i. e.* the classical
acute liver-atrophy, no definite cause has yet been discovered.

The disease may appear at any age and in either sex. In some cases,
parturition seems to be a determining factor, but it does not play the

important part attributed to it by some authors. The condition is associated with the occurrence of jaundice.

Morbid Anatomy.—In the early stages, it is said that the liver may be slightly enlarged. Very soon, however, it becomes shrunken and flabby. The capsule, on account of the degenerative shrinking of the substance of the organ, becomes wrinkled. On section, a variegated appearance is presented, brownish-yellow or bright yellow jaundiced areas alternating, in a very irregular manner, with bright or dark red patches. These latter are areas in which the liver-cells have become disintegrated, and replaced by dilated capillaries and hæmorrhagic foci—the former, *i. e.* the yellow areas, are the parts where the liver-cells, stained with bile, still survive. The changes are very unevenly distributed, and, though some areas are soft and friable, the section, as a whole, is usually somewhat firm and elastic. The gall-bladder generally contains only a small quantity of bile, or the contents may be colourless and be composed mainly of mucus; but there are no special changes in the gall-bladder itself or in the larger bile-ducts.

On microscopical examination, the liver-cells shew all stages of degeneration. At the beginning of the process, the cells are swollen, and more granular than normal. Gradually, the nucleus loses its power of staining with the basic dyes, the cytoplasm becomes disintegrated, and the outlines of the cells indefinite—irregular, granular masses and débris remaining as the only residue of the degenerated liver-cells. Eventually, even this débris is absorbed, and the lobules of the liver are represented by masses of capillaries and the supporting structures. In these degenerated areas, crystals and granules of pigment, hæmatogenous in origin, are found, and also, sometimes, leucine and tyrosine. In some of the less acute cases (**subacute liver-atrophy** or **subacute yellow atrophy**), regenerative processes in the liver-cells are seen side by side with the degenerative ones.

In the portal tracts in both acute and subacute cases, there is usually an apparent proliferation of the minute bile-ducts. According to Lindsay Milne,[1] these "duct-structures" are not produced by proliferation, from either liver-cells or bile-ducts, but are simply "the becoming evident of the normal more resistant bile-channels connecting the liver-cell with an inter-lobular bile-duct." "Their epithelium tends to assume a cubical appearance in the same way as does the delicate lining of the air alveoli of the lung in interstitial pneumonia."

Numerous petechial hæmorrhages are generally found in the skin and in the serous and mucous membranes. The urine may contain leucine and tyrosine.

(c) **POISONING with TRI-NITRO-TOLUENE (T.N.T.),**[2]**etc.**—A condition very similar to **acute liver-atrophy** has been described as occurring among

[1] Lindsay Milne, *Brit. Med. Jour.*, October 17, 1908, p. 1169.

[2] T.N.T., either pure or compounded with ammonium nitrate (amatol or ammonal), may be absorbed through the skin or through the digestive tract, or by inhalation of its fumes or dust. It may cause dermatitis, neuro-vascular conditions, gastro-intestinal disturbances (especially gastritis and constipation), and occasionally, a very fatal form of anæmia (aplastic anæmia), as well as the liver-degeneration or "toxic jaundice" described above.

munition- and aeroplane-workers—in the former, because of the use of **tri-nitro-toluene** and its compounds, and in the latter, because of the presence of **tetra-chlorethane** in the " dope " or cellulose varnish which was at one time used for coating the wings of aeroplanes. The liver, in these cases, is considerably reduced in size and may shew an irregular surface with the capsule wrinkled and thickened. On section, it presents a mottled appearance, red and yellowish or greyish areas being irregularly distributed, and the yellowish areas projecting above the reddish ones.

On **microscopical examination,** the liver-cells shew all stages of degeneration, the most marked changes being near the centres of the lobules. The cells may be swollen, granular, or fatty, but a great many of them are necrosed and only débris left. The amount of fatty change varies in different cases. This, no doubt, depends on the intensity of the poisoning—the more acute and rapid cases shewing only destructive and necrotic changes in the cells. The yellow areas represent the less advanced changes. In the red areas, there may be no trace of liver-cells, the tissue present representing the walls of the capillaries and also developing fibrous tissue. This new fibrous tissue varies in amount and in the stage of development, and certain areas may be completely fibrous. Cellular infiltration in the portal spaces is sometimes a marked feature— the cells being of the lymphocyte-type and representing the early stage in the cirrhotic condition. The small bile-ducts around the portal tracts may appear to be more numerous than normal, and they frequently shew catarrhal changes. Areas of regeneration are sometimes seen. The left lobe of the liver is usually more affected than the right. These degenerative changes are due apparently to the direct action of the poison on the cells of the liver, and not to any special haemolysis. The jaundice results, in part at any rate, from the obstruction caused by the catarrh in the small bile-ducts. The blood, in this condition, may not shew any special changes, but there is frequently a diminution in the number of leucocytes, though, in some cases, there is an actual increase of these cells. Fatty and other degenerative changes may also be found in the secreting cells of the kidney and in the myocardium.

(*d*) **CLOUDY SWELLING** of the liver-cells occurs in connection with all acute bacterial and toxic diseases. There is, usually, a preliminary congestive stage which, however, generally passes off as the capillaries become compressed between the swollen liver-cells. The liver is enlarged, and the hepatic cells appear more granular than normal. This granularity (p. 30) is largely due to a swelling of the cyto-reticulum. Albuminous and fatty granules may be present. The liver-tissue is paler and more opaque than normal, the outlines of the lobules are obscured, and the substance is more friable.

(*e*) **FATTY CHANGES** are common, both degeneration and infiltration occurring, very frequently in combination (*see* Plate I, figs. 1 and 3, p. 42). They are found especially in acute fevers, in septicæmia,

in wasting diseases, in acute alcohol-, phosphorus-, or chloroform-poisoning, in severe anæmias, especially pernicious anæmia, etc. They may follow, and be associated with, cloudy swelling. For descriptive purposes it is convenient to describe **Fatty Degeneration** and **Fatty Infiltration** separately.

Fatty Degeneration.—The liver may be slightly enlarged, but, more usually, it is reduced in size. The substance is friable, and pale or yellowish —being, in acute cases, sometimes bright canary-yellow in colour. **On microscopical examination,** the hepatic cells are found to be filled with minute droplets of fat, which are irregularly distributed throughout the cytoplasm—the nucleus of the cell remaining more or less central. In the earlier stages of the process, the fat-globules are, in some cases, found specially towards the central part of the lobule, round the hepatic vein. Very often, however, the distribution of the change is throughout the lobule, a condition which is also seen in the later stages of cases in which it originally has been central. The particles of fat are usually small, but, especially in the more acute cases, they may coalesce to form larger globules.

Fatty Infiltration.—In uncomplicated fatty infiltration, the liver may be increased in size, often to a considerable extent, and its edges rounded. The organ is unduly soft in consistence, and has a yellowish colour. In the earlier cases, especially if combined with chronic venous congestion, the lobules may be mapped out very distinctly, the pale yellowish periphery being in marked contrast with the red centre. In more advanced uncomplicated cases, the lobular outline is lost. **On microscopical examination,** the fat is seen in the form of large globules, especially in the peripheral zone of the lobule; but, as the condition advances, the fatty droplets are, as a rule, found in all the cells from the periphery to the centre. The cells are swollen, and the nucleus is pushed to one side as a result of confluence of the globules. This condition is seen especially in cases of chronic alcoholism. Its occurrence in combination with chronic venous congestion has already been described. The condition is always associated with a varying degree of fatty degeneration.

(f) **WAXY** or **AMYLOID DEGENERATION** in the liver is always associated with waxy degeneration in the spleen and the kidney, and perhaps also in other organs. The fine connective tissue in the walls of the hepatic artery may alone be affected, or the condition may be wide-spread, and affect almost the whole of the capillary network of the organ. All stages between these two varieties may be found. The liver is enlarged, sometimes very considerably, and the edges are rounded. It is firm and elastic in consistence. **On section,** there is a wax-like translucence of the whole surface or, in some cases, of irregular areas. **On microscopical examination,** there is great thickening of the walls of the arteries and capillaries, the thickened tissues presenting a homogeneous, translucent appearance, and reacting with the special stains for waxy

degeneration (*see* Plate II, fig. 3, p. 58). The intervening liver-cells are greatly atrophied, and, in places, may have entirely disappeared. Fatty degeneration is frequently associated with the waxy change. The change spreads sometimes to the walls of the portal and hepatic veins, and to the connective tissue of the portal tracts. In spite of the very great thickening of the walls of the vessels, there is little, if any, obstruction to the blood-flow through the liver, and, consequently, no ascites. There is no hindrance to the outflow of bile, and, therefore, jaundice is not associated with the waxy change.

(*g*) **PIGMENTARY CHANGES.**—An increased amount of pigment may occur in the liver-cells in various diseased conditions. In all cases

FIG. 363.—*Waxy or Amyloid Degeneration of Liver.* The lower parts of each section have been treated with iodine. Three specimens showing different types of distribution of the change.

of **atrophy** of the liver, an increase in pigmentation is found. In diseases in which there is breaking down of the red blood-corpuscles, the hæmato-genous pigment accumulates in the liver-cells. This pigment may contain **iron,** either in loose, or in firm, combination. Thus, in pronounced **anæmias,** especially of the **pernicious** type, in **septicæmias,** etc., a pigment—hæmo-siderin—which gives the chemical reactions of free iron, may be found in considerable quantities, especially in the peripheral zone of the lobules (*see* Plate III, fig. 3, p. 74). In **chronic venous congestion,** the pigment is deposited in the cells of the central zone, and, in this hæmatoidin pigment, iron cannot be demonstrated by the ordinary chemical tests.

In cases of **malaria,** a pigment derived from the red blood-corpuscles accumulates in the connective tissue of the portal spaces, along the walls of the capillaries, and in the liver-cells. In **hæmochromatosis,** there may

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be a very considerable amount of pigment—iron-containing (hæmosiderin) and iron-free (hæmofuscin) in both the liver-cells and the connective tissue. In **jaundice,** the bile-pigment, in the form of dark green granules or in crystalloid masses, accumulates both in, and external to, the liver-cells, giving to the liver a dark olive-green appearance (*see* Plate III, fig. 5, p. 74). In cases of poisoning with **salts of silver,** there may be an accumulation of the silver in the liver-cells. Sometimes, though very rarely, carbon-pigment is found in the portal spaces in cases of **anthracosis.**

(*h*) **GLYCOGENIC INFILTRATION** occurs, but has been sufficiently referred to in Chapter II, p. 53.

(*i*) **FOCAL NECROSIS** in the liver is dealt with in Chapter III, p. 98.

"INFLAMMATION OF THE LIVER" :—

Acute inflammatory changes in the liver, apart from abscess-formation, are said to occur commonly in tropical countries, and especially in cases of malaria. Reference has already been made to **Acute Congestion** and to **Cloudy Swelling.**

SUPPURATIVE HEPATITIS (Abscess of the Liver) occurs in various forms :—

(*a*) **TROPICAL ABSCESS** is sometimes found without active symptoms of dysentery, though in some of these cases, ulceration of the intestine is present. As a general rule, however, the presence of dysenteric ulceration is indicated by definite clinical manifestations, and the abscess is a **secondary manifestation of the ulceration.** The abscess in the liver is most frequently a solitary one, but two or more abscesses may be present, occurring in series, so that, on *post-mortem* examination, each may shew a different stage in the process of development. The abscess usually takes origin deep in the substance of the liver, and may gradually make its way to the surface of the organ, there giving rise to the formation of sinuses which open through the diaphragm or through the abdominal wall. The contents of the abscess, thick, creamy, and of a pinkish colour, consist of fragments of broken-down liver-tissue, with or without pus-cells. There may be no sign of inflammation in the surrounding tissue, but, in chronic abscesses, the wall shews a very definite formation of cicatricial fibrous tissue. **On microscopical examination,** *Entamœbæ histolytica* may, or may not, be found in the contents of the abscess; but, in the necrosing liver-tissue forming its wall, they are always present and often in considerable numbers. The amœbæ may also be found in vessels at some distance from the local focus. Secondary infection with various bacilli, especially those of the colon-typhoid group, and micrococci, is not infrequent. The amœbæ pass to the liver from the intestine by way of the portal vein and its tributaries.

(*b*) **PYÆMIC ABSCESSES** are usually multiple, and may be widely spread in the liver, or localised to definite areas. They are commonly secondary to a septic phlebitis of the portal vein—the source of the infec-

tion being usually in the large intestine and appendix, and frequently causing, in the first instance, a septic thrombosis of one of the mesenteric veins. A similar condition is sometimes produced by direct thrombosis of the vein, which may arise as a result of ulceration into it, or of pressure on it, by a gall-stone impacted in the bile-ducts, or of the severe inflammatory changes which may follow this cause, even where ulceration has not taken place. On the other hand, abscesses occur without thrombosis. Thus, in cases of pyæmia, the causal bacteria which are in the blood may become lodged in the liver, and give rise to abscess-formation. **On microscopical examination,** the contents of the abscess are seen to consist of degenerated and necrotic liver-tissue mixed with leucocytes of various kinds. The causal bacteria may also be found.

(c) **BILIARY ABSCESSES,** or collections of pus in the biliary passages, result from retained secretion in the passages becoming infected, the obstructing agents being gall-stones, cancer, parasites, etc. In other instances, there may be a diffuse suppurative condition of the bile-passages **(suppurative cholangitis).** The infecting organism is usually one of the members of the colon-typhoid group.

(d) **Abscesses of the Liver** due to infection with *Streptothrix actinomyces*, or resulting from **suppuration** in **hydatid cysts,** and other causes, may also occur, but present no important features which distinguish them from similar abscesses elsewhere.

CHRONIC INTERSTITIAL HEPATITIS (CIRRHOSIS) :—

The pathological manifestations of this group of diseases vary, but, in all cases, the essential change is an overgrowth of the supporting connective tissue of the organ— the new formation commencing almost always in the region of the portal spaces, where the fibrous tissue is normally most abundant. This increase of fibrous tissue may be confined to the periphery of the lobules, or it may spread into them, and so isolate masses of liver cells.

Causation.—The disease is usually the result of irritants carried to the liver by the blood, the nature of these irritants often being obscure. **Alcohol** in certain forms seems to be a very potent factor—the ordinary " gin-drinker's liver " being a definitely recognised form of the disease. We have, however, seen cases in which the liver exhibited changes identical with those found in this variety of cirrhosis, where all possibility of alcoholic indulgence could be excluded; and Greenfield and others have described the occurrence of a similar condition in the liver of the cat. The condition may occur **secondarily to infective diseases,** such as **leprosy, syphilis, malaria,** etc., and a similar cirrhotic change in the liver may be found in young subjects, especially after **scarlet fever.** In the cirrhosis of **bronzed diabetes** or **hæmochromatosis,** the irritation caused by the pigment seems to be an important agent in producing the overgrowth of the fibrous tissue.

Irritation of the biliary passages in the liver also brings about this overgrowth, and it has been said—though there is little evidence in support of the statement—that the direct passage from the intestine, by way of the bile-passages, of bacteria, the products of bacterial activity, or the products of disordered intestinal metabolism, may have some share in the production of **biliary**—or what Mallory calls "**infectious**"—**cirrhosis.** In the majority of cases, it seems more probable that the irritation is brought about by toxic substances which reach the bile-passages directly from the blood-stream. The distribution of the fibrous tissue in the liver is determined by the nature of the irritant, the manner of its introduction, and probably, to a greater degree, by the extent and characters of the lesions produced by it—especially its effects upon the liver-cells.

For many years, pathologists have regarded this **fibrous-tissue overgrowth** as the primary lesion in cirrhotic conditions of the liver; but recent researches, especially those in which experimental methods have been employed, conclusively prove that, though such " irritative " overgrowth may result, to a certain extent, from the direct action of the irritant upon the pre-existent fibrous tissue, yet the **essential and most important action of the toxic substances is on the liver-cells themselves.** According to the rapidity or chronicity of the destructive changes **in the liver-cells,** according to the extent and distribution of these changes, and according to the capacity or otherwise of the cells to undergo regenerative and reparative processes, so will be the nature and distribution of the resulting histological lesions.

Thus, in the so-called " acute liver-atrophy," the destructive processes in the liver-cells are rapid, wide-spread, and in excess of the reparative. In " subacute liver-atrophy," which is due usually to **recurring** acute attacks of less severity, the patient survives long enough to allow of a considerable amount of repair to take place. In multilobular cirrhosis, due to the action of some toxic substance such as alcohol, the damage to the liver-cells is long continued and gradual; and it is the cells at the periphery of the lobules that are, from their position, specially liable to such damage. Many of them are destroyed, and, if they are not replaced by proliferation of the liver-cells themselves—a process which is usually, in such cases, somewhat imperfect—their place is taken by the tissue which can most readily undergo proliferation, viz. the connective tissue of the portal tracts, which, accordingly, gradually and progressively replaces them.

Thus, to sum up the position : though, in some cases of fibrous overgrowth in the liver, it must be admitted that the irritant acts directly on the connective tissue, causing it to proliferate, there seems no doubt that, in the majority of cases, the primary change is a destruction of the liver-cells. This is followed by a certain degree of regeneration, which, however, is inadequate to the needs of the organ; and, as a sequel, what may be

regarded as a compensatory, or rather complementary, overgrowth of fibrous tissue takes place.

COMMON CIRRHOSIS (Polylobular or Multilobular Cirrhosis, Alcoholic or "Hobnail" Cirrhosis, "Gin-Drinker's Liver").— In this form of cirrhosis, the overgrowth of fibrous tissue appears to be related especially to the distribution of the portal vein in the liver.

In the more **acute manifestations** of this disease, the newly-formed fibrous tissue may be wide-spread in its distribution, and extend for some distance into the peripheral part of the lobule. The liver is usually enlarged, and shews very slight irregularity of surface—in fact, in the early stages of the process, the surface is comparatively smooth. **On section,** the fibrous tissue is widely spread and somewhat cellular in character, and it isolates areas of liver-tissue which vary considerably in size — some corresponding with single, some with several, lobules. There is extension of the fibrous tissue into the peripheral zone of the lobules, with also a proliferation—or an apparent proliferation [1]—of the small bile-ducts. Fatty changes are almost constantly present in the liver-

FIG. 364.—Common or Polylobular Cirrhosis of the Liver, shewing "hobnail" appearance of the surface.

cells. This condition is frequently associated with jaundice, and hence is often classed with the **"Hypertrophic Cirrhosis"** of Hanot.

Usually, the condition is **chronic,** and constitutes the form of

[1] *See* pp. 791 and 798 for Lindsay Milne's interpretation of these apparently proliferative changes.

atrophic cirrhosis or "**hobnail**" **liver.** The liver, which at first may be slightly enlarged, soon becomes contracted, irregular on the surface, and extremely hard. The elevations, which are composed of areas of liver-cells, are often yellow in colour from fatty changes. **On microscopical examination,** there is marked proliferation of the fibrous tissue round the inter-lobular branches of the portal vein. This fibrous tissue is dense in character, and usually surrounds **several** lobules of the liver, hence it is termed **multi-** or **poly-lobular cirrhosis.** Some invasion at the margin is usually seen, and thus, small, irregularly rounded areas of liver-tissue

FIG. 365.—Common or Polylobular Cirrhosis of the Liver. ×25.

become isolated. The liver-cells shew fatty and other degenerative changes, and may, in certain areas, be extensively atrophied. Mallory [1] describes a form of **necrosis of the liver-cells,** which he claims is character-istic of alcoholic cirrhosis. The cells are swollen, and an irregular, coarse, hyaline network appears in them. This may occur at scattered points in, or be widely diffused throughout, the liver. After the hyaline change has reached a certain degree of intensity, the cells become surrounded and invaded by numerous polymorphonuclear or mononuclear leucocytes, which dissolve the cell and bring about its disappearance. Side by side

[1] Mallory, *Principles of Pathologic Histology,* W. B. Saunders Company, 1914, p. 504.

with the destruction, active regeneration takes place, and a proliferative activity of the fibroblasts leads to the increase of connective tissue. In practically all cases, atypical areas of liver-cells, in which the cells are grouped in thick irregular columns, are seen; and, in these, the individual cells may be of considerably larger size than normal, and may shew mitotic figures. These are areas of regeneration, and are probably compensatory in nature. It is still uncertain whether the newly-formed liver-cells originate from bile-duct epithelium or from pre-existing liver-cells, the latter being their more probable origin. The bile-ducts may shew a certain degree of proliferation, but are not obstructed, so that jaundice is not a usual result of this form of cirrhosis. There is considerable obstruction to the flow of blood through the portal vessels, and, unless such supplementary channels as the ductus venosus or remnants of the umbilical veins are patent, or unless anastomosing channels between the vessels in the diaphragm and those in the capsule are established, an accumulation of fluid takes place in the abdomen (ascites). Attempts to establish this collateral circulation by the production of adhesions between abdominal wall, the capsule of the liver and the omentum have been made by surgeons.

The veins at the cardiac end of the stomach become dilated and varicose, and rupture of these is one of the common causes of hæmorrhage from the stomach in this condition. Hæmorrhage from the rectum is more frequent, and is due to the rupture of varicose hæmorrhoidal veins.

Associated with the cirrhosis, there is very frequently catarrh of the stomach and the intestine. The spleen is generally enlarged, and its capsule thickened.

BILIARY CIRRHOSIS.—This condition usually results from obstruction to the outflow of bile. The retained substances, acting as an irritant, bring about proliferative overgrowth of fibrous tissue, especially round the obstructed passages. The causes of the obstruction may be calculi, stricture, pressure from without by glands or tumours, etc. A prolonged catarrhal condition, as a result of the passage along the ducts of bacteria or other infective agents, may also bring about obstruction, and the form of **hypertrophic cirrhosis of Hanot** is generally attributed to such a cause. Persistent jaundice generally occurs. The affected liver is usually enlarged—sometimes considerably so—the enlargement being uniform. The surface is either smooth or only slightly granular. **On section,** the liver is deeply bile-stained, the consistence is firm, and an overgrowth of fibrous tissue is present. **On microscopical examination,** the fibrous tissue is seen to enclose small areas of liver-tissue—mostly single lobules (**mono-lobular**)—and to send delicate strands into the lobules. The bile-ducts are generally dilated, and the bile-capillaries appear to shew evidence of multiplication, though, as has been already stated, Lindsay Milne suggests that this appearance is to be interpreted as due rather to swelling of the flattened endothelial-like cells lining the minute biliary channels running
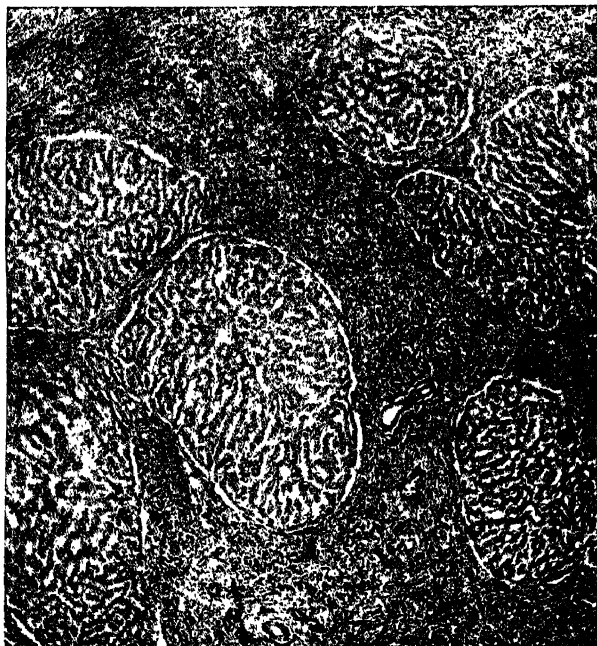
FIG. 366.—*Liver.* Monolobular Cirrhosis, shewing the isolation of small areas of liver-cells by the newly-formed fibrous tissue.   × 60.
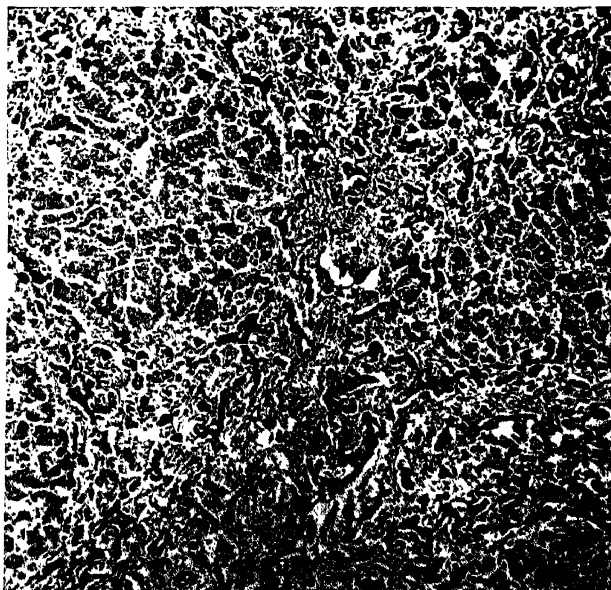
FIG. 367.—*Liver.* · Biliary Cirrhosis, shewing the apparent increase in the bile-ducts in the newly-formed fibrous tissue.   × 60.

between the columns of liver-cells, a process which occurs as the intervening liver-cells at the periphery of the lobule are destroyed. These biliary channels are thus rendered more prominent, and their cells become more or less cubical in shape—a change analogous to that occurring in the endothelial lining of the pulmonary alveoli in chronic interstitial pneumonia. In this variety of cirrhosis of the liver, the fibrous tissue is usually less in amount and more delicate than in polylobular or common cirrhosis. In certain cases, especially where the obstruction is absolute, decomposition-changes may take place in the bile, and a necrosis of the liver-cells, simulating acute liver-atrophy, may follow.

MALARIAL CIRRHOSIS is usually described as being monolobular in type, with the liver small and very irregular in its appearance, resembling the condition seen in alcoholic cirrhosis. By some authors, this form of cirrhosis, which undoubtedly occurs in certain cases of malaria, is regarded as quite independent of, and not caused by, the continued malarial attacks. It is practically impossible, in any given case, to exclude all the other possible and well-recognised causes of cirrhosis, and, therefore, the actual proof of the existence of a definite "malarial cirrhosis" cannot, as yet, be regarded as definitely established.

CIRRHOSIS DUE TO KALA-AZAR was described, in 1908, by Leonard Rogers, who found varying degrees of the condition in about one quarter of all cases of this disease. In a series of adult cases of **chronic** kala-azar, investigated by Nattau-Larrier in India, it was found that the hepatic fibrosis might be either insular or diffuse, the latter form being a fine peri-capillary fibrosis, closely resembling the inter- or mono-cellular cirrhosis of congenital syphilis (*see* below). The parasites may be demonstrated in the fibrous tissue of the lesions.

CIRRHOSIS DUE TO FLUKE-WORMS.-- Secondary fibrosis may spread into the liver-tissue from the infected bile-ducts, in cases of helminthiasis due to *Fasciola hepatica* (*Distoma hepaticum*), as reported by Fischer in China; and cirrhotic changes have also been described in infections of the portal veins with *Schistosoma japonicum*.

CIRRHOSIS FOLLOWING PERIHEPATITIS may affect the superficial parts of the liver-tissue. The capsule may be much thickened, and the fibrous bands, passing from it into the substance of the liver, may produce atrophy of the cells.

SYPHILITIC DISEASE OF THE LIVER :—

The changes in the liver in syphilis are usually very marked, and vary somewhat, according to whether the disease be congenital or acquired.

Congenital Syphilis, may, in infants, manifest itself specially in the liver, which is usually enlarged, and smooth on the surface. On naked-eye examination of sections, **gummata,** usually of small size, may be seen, and there are often present, in addition, rounded translucent areas which are connected with the hepatic artery. **On microscopical examination, diffuse**

interstitial hepatitis is seen, the newly-formed connective tissue being highly cellular, and appearing to develop first between the liver-cells and the endothelium of the capillaries. The lobular outlines become indistinct, and the radiate arrangement lost—the cells being separated into small, isolated clumps by the diffuse spread of the fibrous tissue, —producing the so-called **monocellular cirrhosis** of Charcot. **Gummata,** having a structureless, caseous centre, or represented merely by cellular foci, may be present, and the translucent areas, referred to above, are seen to be nodules of granulation-tissue associated with **end-arteritis** or **peri-arteritis** of the hepatic arteries. In children which survive for a few
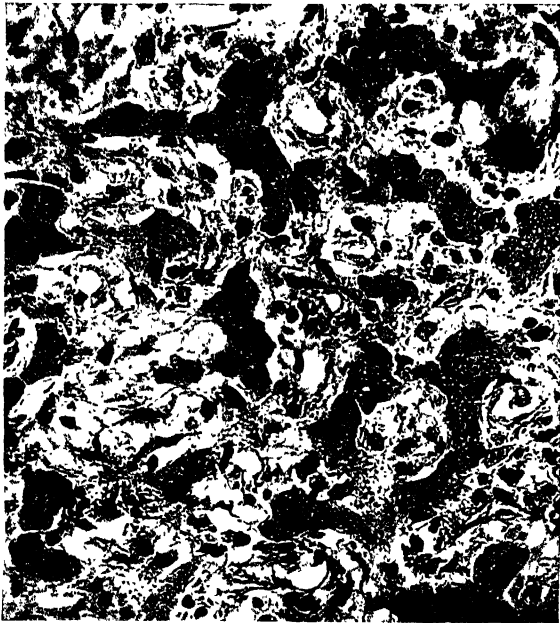
Fig. 368.—*Liver.* From a case of Congenital Syphilis, shewing diffuse over-growth of connective tissue (inter-cellular cirrhosis). × 300.

months or longer, fibrous cicatrices—producing "lobed" rounded masses—waxy degeneration, and perihepatitis, may also be found. In and around the miliary gummata, in the young granulation-tissue round the vessels, in the walls of the vessels, and in and around the liver-cells, the characteristic spirochætes of syphilis (*Spirochœta pallida*) are seen, sometimes in enormous numbers.

Acquired Syphilis.—In this condition, the changes are usually more localised than in the congenital form, and are especially marked towards the superficial parts. The usual evidence of this form of syphilis is the presence of **cicatrices,** especially near the suspensory ligament. In some cases, the cicatrices are very numerous. At the bottom of these cicatrices, **gummata,** varying in size, and fibrous bands spreading

into the neighbouring liver-tissue, are often seen, though, in old-standing cases, they may become entirely absorbed and replaced by fibrous tissue. The gummata almost always shew a caseous centre, surrounded by a zone of fibrous tissue. **Perihepatitis** is sometimes present in an extensive degree, frequently giving rise to firm fibrous adhesions between the liver and the diaphragm, etc.; and the capsule may shew irregular thickening. **Waxy disease,** regular or very irregular in its distribution, is common (*see* fig. 14).

TUBERCULOSIS OF THE LIVER :—

· Tuberculosis of the liver manifests itself in the form of minute greyish granulations, often just visible to the naked eye, and which are seen both in section and in the superficial parts under the capsule. The latter variety may be part of a general miliary tuberculosis, or of a localised tuberculosis of the peritoneum. These small tuberculous nodules, sometimes bile-stained, are frequently seen in the portal tracts, near, and often involving,

Fig. 369.—Chronic Tuberculous Nodules in the Liver.

the bile-ducts. On **microscopical examination,** these nodules present the usual characters of caseation, etc. Sometimes the granulations are larger—from a sixth to a quarter of an inch in diameter—and irregular in outline. The central part may soften and produce an irregular cavity, the walls of which are often bile-stained. These cavities are the so-called **bile-cysts.** In rare cases, tuberculosis in the liver spreads along the walls of the larger bile-ducts, producing obstruction and jaundice. Chronic tuberculous nodules of larger size, *e. g.* even as large as a hazel nut, though very uncommon in man, are sometimes found (*see* fig. 369.)

ECLAMPSIA.—In this condition, the liver shews characteristic hæmorrhages around the portal vessels and beneath the capsule. These are at first small, but tend to coalesce into larger areas. Fibrin forms round the red blood-corpuscles and is specially abundant close to the portal vessels. Following the hæmorrhage, the injured liver-cells undergo necrosis—which may be focal or central. The focal areas are usually small, and either

mid-zonal in position or adjoining the hepatic or portal vessels; the central necrosis may affect the larger part of every lobule. The necrosis may occur without the hæmorrhages and no definite relation between the the two has been established.

ACTINOMYCOSIS :—

Metastatic abscesses from actinomycotic foci in almost any part of the body are liable to occur in the liver. The parasite seems to be carried by the blood-stream, possibly in the leucocytes. These abscesses may be in the form of multiple granulomatous nodules, but, more frequently, they form definite abscesses which burrow irregularly in the liver—the section of the organ presenting a sponge-like structure. The causal organism, *Streptothrix actinomyces*, may be isolated from the pus or from the necrotic walls of the abscess. The microscopical characters of such nodules and abscesses are described on p. 240.

LEPROSY :—

B. lepræ are usually found in enormous numbers in the endothelial cells of the liver in cases of leprosy, and, in some cases, definite granu-lation-tissue nodules are present (*see* p. 234).

Fig. 370.—*Sarcoma.* Secondary Nodules in Liver.

TUMOURS :—

Angiomas occur, generally on the surface of the organ, as dark red or purplish, slightly elevated areas, which are either encapsuled, or merge gradually into the surrounding liver-tissue. They vary in size, but are usually small and solitary. Occasionally they are multiple, and may be found even in large numbers, not only on the surface, but some-times in the substance of the liver. **On microscopical examination,** the tumours are found to be of the cavernous type (*see* p. 320).

Adenomas are solitary or multiple, and appear as nodular masses, with a varying degree of encapsulation. They are frequently associated with cirrhosis of the liver, though they may occur quite independently of that condition. The cells forming the glandular structure of the tumour resemble those of the hepatic tissue proper, except that they are
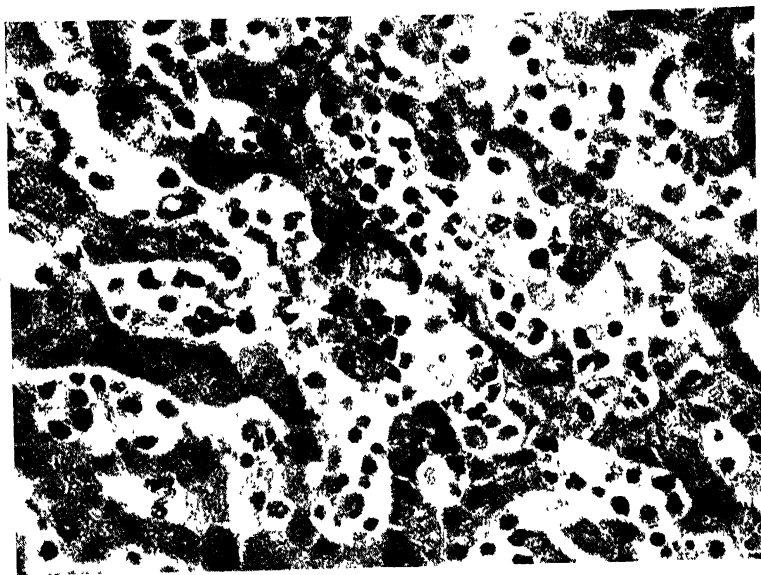
FIG. 371.—*Liver* Medullary Leukæmia, shewing infiltration with myelocytes, etc. × 400.
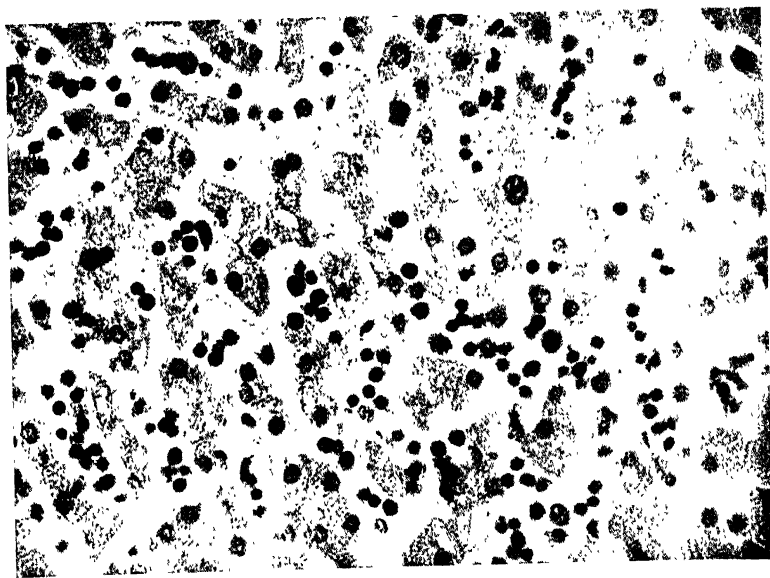
FIG. 372.—*Liver*. Lymphatic Leukæmia, shewing infiltration with lymphocytes. × 400.

usually larger. Some authors hold that these so-called **adenomas** are not true glandular tumours, but merely portions of liver-tissue which have been isolated or newly formed in the cirrhotic process. There seems little doubt that some of the primary malignant growths of the liver have their starting-point in such adenomas (*see* below).

Primary sarcomas have been described, but are very rare; **secondary sarcomas,** especially of the small round-celled and the melanotic types, are not infrequent.

Lymphomatous masses, resembling sarcomas, are seen in the interstitial

Fig. 373.—Primary Malignant Adenoma of Liver, or Liver-celled Cancer.

connective tissue of the liver in some cases of **leukæmia,** and somewhat similar nodules may be found in cases of **lymphadenoma.**

A few cases are on record of **adrenal tissue** being present in the liver, and tumours may arise from this.

Primary Cancer develops occasionally in the liver, sometimes originating in connection with the bile-ducts; though, more usually, it arises directly from the hepatic cells themselves (liver-celled cancers). Of the latter variety, most of the cases occur in connection with cirrhotic conditions of

the liver and some at least, as noted above, have their origin in the so-called simple adenomas.

In tumours of the **bile-duct** variety, the new growth usually forms one or more nodular masses which are adenomatous in type, the glandular spaces being lined by cylindrical, or more irregularly shaped, epithelium. These tumours generally remain localised, but occasionally give rise to secondary growths. Sometimes, the growths are very rapidly produced, and extremely vascular. In the **liver-celled** type, the cells are arranged
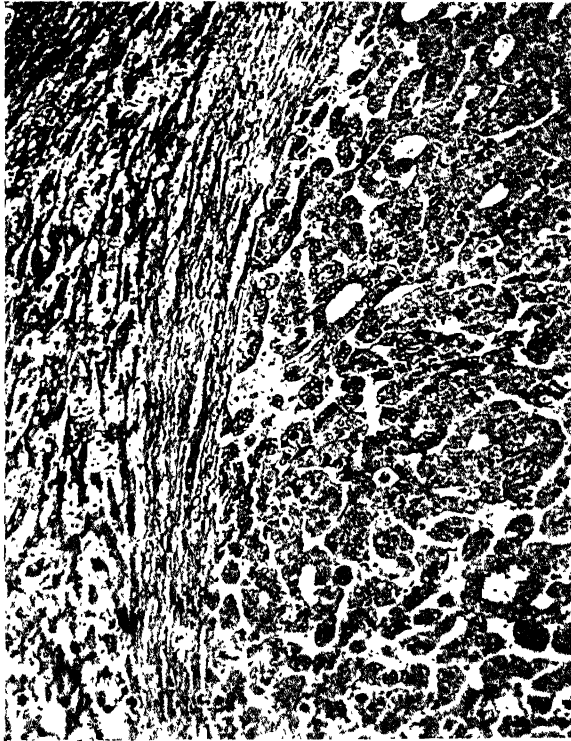
Fig. 374. *—Primary Liver-celled Cancer.* Shewing irregular columns of large cells, resembling those of the liver, but with aberrations in size, appearance of the nucleus, etc. × 100.

in masses or in thick irregular columns, and often shew great irregularity in size and shape, though still maintaining a general resemblance to the liver-cells from which they originate; the surviving liver-tissue, and, in some cases, the tumour nodules, may be deeply bile-stained.

Secondary Cancers, spreading from the gall-bladder, may invade the liver; but most of the secondary growths attacking the liver extend to the organ by way of the portal circulation or by lymphatics, from tumours in the stomach, intestine, etc. The secondary nodules may be very numerous. They are usually irregular in shape, pale in colour, and, if near the surface of the organ, shew themselves as nodular elevations,

with, very frequently, a depressed centre (**umbilication**). On section, the centres of many of the nodules shew a yellowish area of necrosis. Hæmorrhage into the tumour-tissue is of frequent occurrence.

In **microscopical characters**, the secondary growths reproduce the characters of the primary tumours from which they originate—adenomas of the stomach or intestine giving rise to adenomas in the liver, a squamous epithelioma of the œsophagus forming a similar epithelioma in the liver, and so on. **Deciduoma malignum** or **chorion-epithelioma** may give rise to secondary growths in the liver. It is not uncommon to find cancerous infiltration in those portal vessels by which the infective material has been conveyed.

As a result of pressure upon the hepatic cells, upon the bile-ducts, or

Fig. 375.—*Encephaloid Cancer.* Secondary Nodules in Liver. The large nodule shews central necrosis.

upon the portal vessels, **atrophy, jaundice,** and **ascites** may occur in cases of extensive tumour-growth in the liver; though, in some cases, there may be very extensive destruction of liver-tissue without jaundice or ascites being present.

CYSTS IN THE LIVER :—

It is not common to find **true cysts** in the liver, though cystic disease of this viscus is sometimes seen in association with cystic disease of the kidney. Such cysts are usually very minute, but may reach from an eighth to a quarter of an inch in diameter. They always result from the dilatation of small bile-ducts. **Large cystic spaces,** due also to dilatation of the bile-passages, are sometimes seen throughout the liver. Con-genital abnormality at the outlet, or obstruction due to some chronic

inflammatory condition, with or without the presence of calculi, is the usual causal factor in these cases.

Small **pseudocysts** occasionally result from the softening and absorption of necrotic areas of liver-cells. The occurrence of **honeycombing** of the liver from the formation of gas by putrefactive organisms has already been mentioned (p. 796), and cysts due to parasites, *e.g.* hydatids, are described on p. 407.

PARASITES OF THE LIVER :—

Hydatids of the liver have been fully described under **Parasites** (see p. 407). **Abscess-formation,** due to *Entamœba histolytica,* is referred to on p. 802.

Fasciola hepatica (*Distoma hepaticum*), *Opisthorcis sinensis* (*Distoma sinense*), and *Dicrocœlium lanceatum* (*Distomum lanceolatum*) occur in the bile-ducts, and *Schistosomum hœmatobium* (*Distoma hœmatobium* or *Bilharzia hœmatobia*) and *S. japonicum* in the portal vessels. A few cases of coccidiosis of the liver are on record.

DISEASES OF THE GALL=BLADDER AND BILE=DUCTS

ANATOMY :—

The gall-bladder, at its neck, forms an acute angle with the cystic duct. This duct lies in the gastro-hepatic omentum, where it joins the hepatic duct to form the common bile-duct. The terminal half-inch of the common bile-duct is embedded in the wall of the duodenum and ends in the **ampulla of Vater.** This ampulla extends into a papilla which generally projects into the lumen of the duodenum. At its opening into the latter, where the duct is narrowest, it is surrounded by a sphincter which regulates the flow of bile. Two lymphatic glands lie in the gastro-hepatic omentum by the side of the bile-duct, and, if calcified, may be mistaken for gall-stones. The common bile-duct in its second stage lies between the head of the pancreas and the duodenum. The intra-hepatic ducts are formed by the junction of bile-capillaries, and these connect with a fine intra-cellular network of channels which surround the nucleus of the cell, but do not enter it. The mucous membrane of the gall-bladder has a reticulated appearance, is lined by columnar epithelium, and secretes mucus. In the ampullary part of the common bile-duct, there are submucous glands lying in crypts and folds, which are liable to infection and inflammation.

JAUNDICE.—This is not a disease, but merely a symptom, and the pathological lesions associated with it are of some importance. The general or localised pigmentation which results from it is dealt with on p. 79.

In obstruction of the bile-duct, distension, extending even into the fine

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'intra-cellular channels, is present in varying degree. The bile is absorbed by the lymphatics, and makes its way into the hepatic blood. The obstruction may be caused by foreign bodies or growths in the passages— e. g. gall-stones, tumours, etc.—new growths pressing on the ducts from outside, stricture or obliteration of the duct, or obstruction at the opening into the duodenum by catarrhal conditions.

Catarrhal Jaundice.—In this condition, there is usually gastro-duodenal catarrh and an extension of this up into that part of the common bile-duct which is embedded in the intestinal wall. The mucous membrane is swollen, there is frequently a plug of inspissated mucus filling the ampulla of Vater, and the narrow part of the duct at its opening into the duodenum. The papilla may be œdematous and congested. This condition of catarrh of the duodenum and lower end of the bile-duct is attributed to errors in diet, to cold, etc. It is, however, so frequently associated with infective fevers, such as pneumonia, typhoid fever, paratyphoid, etc., that there seems reason to believe that many of the cases of jaundice which were supposed to be due to errors of diet, etc., are really infective in origin. As we have already stated, there are crypts and folds in the ampullary part of the common bile-duct, and, in these crypts, bacteria are likely to collect. Examination of the bile-passages in "Carriers" of typhoid, paratyphoid, etc., prove the occurrence of the bacteria in the ducts and in the gall-bladder. The frequency with which jaundice occurs in typhoid and paratyphoid fever has led some authors to describe this form under the name of **Enteric Jaundice.** Duodenal catarrh is present in these cases, and there seems no reason to regard this condition as other than a variety of catarrhal jaundice of bacterial origin. The duodenitis may be very marked, and the catarrhal condition in the bile-passages may extend to the gall-bladder. The condition may occur in epidemic form, and the clinical features so closely resemble those seen in the form of jaundice called **Spirochætosis ictero-hæmorrhagica (Infective Jaundice),** that many of the cases which have been attributed to "enteric" infection may have been of this nature. At the same time, there can be no doubt that jaundice of a severe type may arise as a result of infection with *B. typhosus, B. paratyphosus A. or B.* and, though less frequently, *B. dysenteriæ;* and their morbid anatomy is so similar that, in the absence of bacterial, serological, or protozoölogical evidence, it is practically impossible to differentiate between any of these conditions. In true enteric cases, the evidence seems to point to duodenal catarrh, with spread of the catarrh into the bile-passages, as being a very common occurrence. This catarrh may be severe and hæmorrhagic and, in some cases, is associated with a hæmorrhagic gastritis.

Infective Jaundice.—An infective jaundice of children has been described, and attributed to a destruction of liver-cells and a setting free of pigment from them. A considerable number of cases of infective jaundice have, during the late war, been described as occurring among soldiers.

Bertrand Dawson and W. E. Hume [1] state that, in the latter cases, the mucous membrane of the **duodenum** is very congested and œdematous. They attribute the obstruction to the swelling of the papilla. The **bile** is very thick and viscous. The **spleen** and **pancreas** shew no pathological changes of importance. In the **kidneys,** hæmorrhage occurs into the tubules; and the presence of sub-pleural hæmorrhages, and hæmorrhages extending into the **lungs** for about one inch, are very characteristic changes. The **liver** is bile-stained, but shews no other pathological changes. In cases described by Stokes, Ryle and Tytler,[2] however, the liver, though not enlarged, or altered in its consistence or colour, shewed, on microscopical examination, irregular areas in which there was degeneration of the liver-cells, collections of polymorphonuclear leucocytes, and an accumulation of bile-pigment. In all their cases, there were multiple petechial hæmorrhages in the peritoneum, pleura, pericardium, and in the heart-muscle, especially in the sub-endocardial region. The kidneys were large, swollen and congested, and shewed multiple hæmorrhages into the tubules. In some of their cases, the intestine and the bile-passages appeared to be normal, but, in others, there were patches of congestion in the mucosa, especially of the duodenum. These writers, however, do not describe the extreme congestion noted in Bertrand Dawson's cases.

C. J. Martin [3] states that in the form of infectious jaundice seen in Gallipoli, there was a systemic infection presenting close analogies to the severe form described by many observers as *Spirochætosis ictero-hæmorrhagica*, but that there was no evidence that the condition was due to a catarrhal condition of the bile-ducts, or an extension of an inflammatory condition from the duodenum, as is usually the case in the jaundice due to paratyphoid infections.

The reports of various observers, on the cases of infective jaundice, point conclusively to a definite infection in many cases with a **spirochæte** which seems to be identical with the *Spirochæta* (or *Leptospira*) *ictero-hæmorrhagiæ* (*see* p. 366) isolated by Inada, Ido and others [4] from an epidemic and endemic disease characterised by fever, jaundice, hæmorrhage, etc., and known as **Weil's disease, febrile jaundice,** etc., to which they have given the name **Spirochætosis ictero-hæmorrhagica.** The spirochæte is present in the blood in the early stages of the disease, but in small numbers, and is entirely absent in the later stages. It has been found in the liver, spleen, lymphatic glands, intestinal wall, adrenals, the bone-marrow, and kidneys, at autopsy; but careful search often fails to reveal the organisms. They may be very numerous in the kidney and may be found during life in the urine.

If, during the first seven days of the illness, the blood from a typical

[1] Dawson and Hume, *Quarterly Journal of Medicine,* vol. x., 1916–1917, p. 90.
[2] Stokes, Ryle and Tytler, *Lancet,* January 27, 1917, p. 142.
[3] Martin, *Brit. Med. Jour.,* 1917, pp. 455.
[4] Inada, Ido, Hoki, Kaneko, Ito, *Jour. Exper. Med.,* vol. xxiii., No. 3, 1916, p. 377.

case is injected into a guinea-pig, the animal develops albuminuria, conjunctival congestion, jaundice and hæmorrhages; and the spirochætes are found in the blood, and may occur in large numbers in the liver. The pathological conditions found in the infected guinea-pig are comparable with those found in the human subject, but the hæmorrhage is more severe and more wide-spread in the lungs of the guinea-pig than in man, and the spirochætes are always found in the guinea-pig when the inoculation gives a typical result. The spirochætes in the blood are always extra-cellular, and in the organs they are rarely found in epithelial or phagocytic cells, but are present in the interstitial tissues.

In the type of the disease seen in France, the tendency to hæmo-rrhage is somewhat less marked than that found in Japan. Pagniez, who prefers, therefore, to call the condition, as it occurs in France, **Spirochætosis icterigenes,** attributes the hæmorrhages to certain changes which he found in the blood, such as prolongation of the coagulation-time, diminution in the number of platelets, and irretractibility of the clot. There is usually a more or less marked leucocytosis, which serves to differentiate the condition from Acute Liver-Atrophy.

Jaundice due to Destructive Changes in the Liver-Cells.—Destructive changes in the liver-cells may occur in the types of jaundice already described; but they are not distinctive, and may be present in only a minor degree, or absent altogether. There is, however, a form of jaundice in which the changes in the liver are a prominent feature, e. g. that occurring in **acute liver-atrophy,** where actual necrosis of the liver-cells takes place to a marked degree: in **chloroform-** and **phosphorus-poisoning,** where extreme fatty changes are found : in poisoning by **tetra-chlor-ethane,** one of the constituents of " dope " or cellulose varnish used for the wings of aeroplanes, which brings about fatty degener-ation, followed by necrosis, of the liver-cells : and in poisoning by **tri-nitro-toluene (T.N.T.)** and its compounds, which produces extreme degenera-tion and necrosis in the liver-cells. No doubt, in some of these cases, there is an additional causal factor—the destruction of the red cells, and, in some of the cases in which jaundice is a noted characteristic, this hæmolysis plays a very important part, e. g. in poisoning by arseniuretted hydrogen, snake-venom, etc.

The pathological changes in the liver in these conditions are dealt with on p. 798.

CHOLANGITIS AND CHOLECYSTITIS.—**Inflammation of the bile-ducts** and **inflammation of the gall-bladder** may arise independently of one another, or one may be secondary to the other. Moderate degrees of cholangitis are common—the inflammation in such cases being generally confined to a short portion of the bile-duct extending upwards for about a half to one inch from its opening into the duodenum. The condition is usually one of catarrh, and the swelling of the lining membrane of the duct causes partial or complete obstruction to the outflow of bile, with

consequent jaundice. The condition may spread more widely, and may extend to the gall-bladder.

The **catarrhal form of cholangitis** is generally the result of the direct spread of the inflammatory process from the duodenum; but it may occur as a result of the irritation of gall-stones; and is sometimes found in the smaller ducts during some of the specific fevers, e. g. typhoid, pneumonia, etc. In certain cases, **suppuration** takes place, the purulent material extending widely and involving the gall-bladder, which may become distended with pus—**empyema of the gall-bladder.** In some of these cases of **suppurative cholangitis,** there has been a pre-existing obstruction, with dilatation of the passages, and accumulation of biliary products—these products becoming infected by bacteria derived directly from the intestine or reaching the passages by way of the blood. *B. coli* and *B. typhosus* are among the commonest organisms found in such cases.

During an attack of typhoid or paratyphoid fever, the gall-bladder frequently becomes infected by *B. typhosus* or *B. paratyphosus* —the **cholecystitis** set up being either **catarrhal** or **suppurative.** According to Scheller,[1] the bacilli are found in the form of capillary emboli in the mucous membrane. The bacilli retain their vitality and virulence in the gall-bladder for a very considerable time after recovery from the acute attack, and it is probable that some of the recurrent cases of typhoid and paratyphoid fever are thus to be explained. More important, however, is the fact which has been emphasised by, among others, Dean, Ledingham, and Walker Hall, that the fæces of such patients contain the bacilli, often only intermittently, and that, for years after an attack, these " carriers " are potential propagators of the disease. The source of some serious outbreaks of typhoid fever, especially in asylums, workhouses, and similar institutions, has been traced to these carriers.

GALL-STONES (BILIARY CALCULI).—These are of frequent occurrence, especially in people past middle life, and in those of sedentary habits, but they occur at any age. They are commoner in the female, and are formed in the gall-bladder, either by a process of crystallisation, or merely by a deposition of some substances contained in the bile, or produced by its decomposition. They are composed of cholesterin, bile-pigments, altered mucus, and salts of lime and magnesia, in varying proportions— some being almost pure cholesterol, the majority, however, being composed of a mixture of this substance with bile-pigments. The cause of their formation is obscure, some authors attributing it to the action of bacteria; and it is not unlikely that some of the cases are associated with previous bacterial infection, e. g. old cases of typhoid fever, etc. Stagnation of the bile is, no doubt, an important predisposing cause, and catarrh of the gall-bladder may also play an important part by supplying, as it were,

[1] R. Scheller, *Centralbl. f. Bakt*, etc., Beilage zu Abt. i., Bd. xlii. Referate, October 27, 1908, p. 50.

a " nucleus " of mucus and shed epithelium, round, and in, which the bile-pigment, etc., may collect.   The calculi occur singly or in numbers.

Of Solitary Gall-stones there are two principal varieties :—

(*a*) Ovoid, somewhat translucent masses, smooth or slightly irregular on the surface, and measuring from a half- to three-quarters of an inch in diameter.   These are easily cut or broken, and, on section, do not shew lamination.   They are composed almost entirely of **cholesterol.**

(*b*) Acorn-like masses, from one inch to one-and-three-quarter inches, or even more, in length, and having a smooth surface which is covered with mucus.   These are often dark in colour, and, on section, shew distinct concentric lamination.   They are composed of cholesterin, bile-pigments, etc.

Multiple Gall-stones are much more common. There may be two or

Fig. 376.—*Large Gall-stones.* From case of an elderly female, in which they ulcerated
through into the transverse colon, and were passed *per rectum*—the patient recovering.
(W. E. C. D.'s case, see *Lancet,* July 28, 1906, p. 221.)

three of these, or the numbers may reach hundreds.   If few, they are, as a rule, comparatively large; if numerous, they are small.   They are usually faceted, and the gall-bladder may be completely filled with them. They are brownish-yellow in colour, have a smooth surface, and, on section, present a central darkish nucleus surrounded by more or less regular layers of different colours—the lighter coloured layers being usually cholesterin, the others, combinations of bile-pigment with lime-salts.   Extremely small calculi, composed almost entirely of bile-pigment—**biliary sand or gravel**—may occur in enormous numbers.   Small, soft masses—putty-like in consistence, and usually dark in colour—are of frequent occurrence in the gall-bladder.   They probably represent an early stage in the process of calculus-formation.

The Gall-bladder is sometimes contracted upon the calculi, or a certain amount of bile or of a viscid mucous secretion accumulates around and between them.   The wall of the gall-bladder is, in some cases, much

thickened, and often shews evidence of chronic inflammatory changes; and suppuration supervenes if infective organisms gain access. One or more of the gall-stones may pass into the cystic duct or into the common bile-duct, and give rise to obstruction, dilatation of the ducts, and obstructive jaundice. The calculus, if it reaches the common bile-duct, may pass into the duodenum, probably, in the majority of cases—unless of comparatively small size, when it occasionally makes its way entirely by the lumen of the duct—completing its passage through an opening which is the result of ulceration. Having passed into the intestine, the calculus, if a large one, sometimes produces obstruction. In a similar way, the gall-stone may ulcerate into the transverse colon. In some cases, ulceration takes place posteriorly through the wall of the duct, producing thrombosis of the portal vein, or even an abscess behind the duct, and peritonitis. Peritonitis is also produced by ulceration of the calculus through the wall of the gall-bladder into the peritoneal cavity. Or again, if the calculus become impacted in the cystic, or in the common, duct, it gives rise to considerable irritation, and, in some cases, such an irritated area seems to be the starting-point of cancer, though, in many cases, it is possible that the two conditions, *i. e.* cancer and calculus-formation, may each be due to some unknown common cause.

OBSTRUCTION OF THE BILE-DUCTS.—This condition is caused by the presence in the ducts of gall-stones, hydatid cysts, liver-flukes, etc.: by pressure on the ducts from outside, by tumours, aneurisms of the hepatic artery, enlarged glands, etc.: or by actual stricture of the duct by inflammatory changes, the presence of malignant disease, etc. Actual non-development of the ducts, or obliteration by cholangitis *in utero*, are occasionally met with.

The opening of the common bile-duct into the duodenum being very narrow, and the pressure of the bile being low, very slight inflammatory changes, such as are produced by a spread of catarrhal inflammation from the duodenum, may give rise to obstruction. The results of such obstruction are usually **jaundice,** considerable **dilatation of the ducts** throughout the liver—the amount depending on the position of the obstruction—and, in some cases, the production of **biliary cirrhosis.**

TUMOURS.—The most important of the tumours are cancers, which are generally primary, and originate in the walls of the ducts (p. 815). They are usually adenomatous in type.

Secondary cancers grow round the walls of the ducts, and infiltrate them.

DISEASES OF THE PANCREAS

In its general structure, the pancreas resembles a salivary gland, being made up of a number of glandular acini loosely held together by fibrous connective tissue. The ducts of these acini communicate with the main pancreatic duct (duct of Wirsung), which opens— usually along with the common bile-duct—into the duodenum.

The main function of the pancreas is the production of digestive ferments. According to Bayliss and Starling,[1] the pancreatic secretion contains inactive **trypsinogen,** which, acted upon by the ferment, **enterokinase,** of the intestinal secretion, becomes active **trypsin**--this union between the two ferments taking place in the duodenum. Besides trypsinogen, there are also present in the pancreatic secretion at least two other ferments, **amylopsin,** which converts starch and glycogen into dextrin and maltose, and **steapsin,** which splits up the neutral fats into fatty acids and glycerine.

The exact relations of the pancreas to certain symptoms produced when it is diseased are imperfectly known. **Total extirpation** of the organ is followed by wasting, glycosuria, and polyuria, *i. e.* all the essential symptoms of diabetes mellitus; and these symptoms also arise in certain cases of disease, especially if accompanied by fibrosis of the organ.

Obstruction of the Pancreatic Ducts.—The pancreatic duct (duct of Wirsung) usually ends, along with the common bile-duct, in the ampulla of Vater. An accessory duct (the duct of Santorini) is present in a more or less developed condition in fifty per cent. of people. The latter duct may open directly into the duodenum at a point nearer to the pylorus than the opening of the ampulla, and thus form a second channel by which the pancreatic secretion may enter the duodenum. **Tumours** of the head of the pancreas, **gall-stones** in the common bile-duct, **aneurisms** in neighbouring vessels, and **pancreatic calculi** in the duct itself, may cause occlusion ; and the part of the gland which is drained by this occluded duct may, if the obstruction is prolonged, become hard and shrunken. ' On **microscopical examination,** such areas shew the pancreatic cells largely destroyed and replaced by scar-tissue, the acini having disappeared or having become dilated, and lined by flattened epithelial cells. If the duct of Santorini is patent, the part drained by it may remain healthy. The **islands of Langerhans,** which are not connected with the pancreatic ducts, remain uninjured and, in advanced cases, may be the only intact original glandular tissue left.

[1] Bayliss and Starling, *Phil. Trans. Roy. Soc. Lond.*, 1904, B. 197, p. 25.

Such chronic interstitial pancreatitis, produced by ligature or obstruction of the duct, may not give rise to glycosuria, even though the interstitial changes be very marked. Some authors hold that the **islets of Langerhans** have a special relation to the glycosuria, and state that, when these are fibrosed or rendered functionless in some other way, sugar is found in the urine, but, as long as they are intact, glycosuria does not occur.

Absence or **inadequacy of the pancreatic secretion** interferes with the normal absorption of **fatty substances** in the intestine, and, in such cases, the stools contain excess of undigested fat.

POST-MORTEM SOFTENING, due chiefly to auto-digestion is frequent, and the whole pancreas may become involved. Microscopically, the nuclei in the affected areas do not stain, and the cells undergo shrinkage, so that the connective tissue becomes more evident.

CONGENITAL ABNORMALITIES.—The presence of small **accessory pancreatic glands** in the omentum, mesentery, and elsewhere, is by no means uncommon. They may occur also in the thickness of the gastric or intestinal walls, where they are sources of weakness, and where they may—especially in the case of the intestine—lead to the production of diverticula, at the distal ends of which the small accessory glands may be found on section (Alexis Thomson). In rare instances, **tumour-growth** may arise from these supernumerary glands.

WOUNDS OF THE PANCREAS allow the escape of pancreatic secretion, and this gives rise to necrotic changes in the fat of the omentum, etc. Cases have been described in which the pancreatic secretion has collected in the lesser sac of the peritoneum and given rise to a **pseudo-cyst.**

HÆMORRHAGE INTO THE PANCREAS may occur as minute petechiæ, or in the form of large hæmorrhagic infiltrations. The former occur in purpura, scurvy, and in septicæmic and toxic diseases in general. The latter, however, are more important, and are generally described under the term "**hæmorrhagic pancreatitis.**" In some cases, this condition is due to inflammation, and may, therefore, be a true pancreatitis; but, in the great majority of cases, inflammatory phenomena are not associated with it. Degenerative changes in the cells of the pancreas occur either as a preliminary to, or as a sequel of, the hæmorrhage. The cells are swollen, the cyto-reticulum becomes more prominent, and the chromatin of the nuclei undergoes disintegration or absorption, with resulting loss of nuclear staining. Among the causes of this condition are necrosis resulting from vascular degeneration, and fatty degeneration of the cells produced by alcoholism, toxæmia, etc.; but, in many of the cases, the precise nature of the cause has not been established. The vascular degeneration may be marked, and may shew itself in the form either of atheroma, or of proliferative endarteritis.

Hæmorrhagic Infiltration results from the destructive changes produced by **tumours,** especially sarcomas and cancers; and it occurs,

though usually in a minor degree, as a sequel of **chronic venous congestion** in cardiac disease, pulmonary disease, or cirrhosis of the liver. Further, **scurvy, purpura,** the **infective fevers,** and **phosphorus-poisoning,** though usually giving rise to minute hæmorrhages, may also be the cause of larger extravasations; and hæmorrhages from embolism, and as a result of fat-necrosis, are said to occur. **Injury of the pancreas** may also be a cause of hæmorrhage.

Results.—Death usually supervenes from shock, or from pressure on the cœliac axis. If death is not thus suddenly produced, gangrene and extensive fat-necrosis result, not only in the pancreas but also in the surrounding fat, especially of the omentum, as well as in the adipose tissue in other parts of the body. A chronic inflammatory change, with overgrowth of fibrous tissue, follows in certain cases where the primary hæmorrhagic condition has not proved fatal.

AMYLOID OR WAXY DEGENERATION is rarely found in the pancreas. **FATTY DEGENERATION** is common. **PIGMENTATION** may occur at the seat of hæmorrhages, but is specially marked in cases of " **bronzed diabetes** " or **hæmochromatosis,** and, in such cases, is associated with pigmentation in other organs, in the skin, etc. The pigment, in these cases, is partly in the form of an iron-free compound, but is largely hæmosiderin, and may occur in enormous quantity and give rise to cirrhosis of the organ.[1]

Areas of **NECROSIS,** varying in size, are produced in the pancreas as a result of hæmorrhage or of inflammation; and a special form of this condition occurs, particularly in the fatty tissue of the pancreas and the omentum, and, in severe cases, in the extra-peritoneal, and even in the subcutaneous, fatty tissue. This **fat-necrosis** appears in the form of minute, greyish-white or yellowish-white, opaque foci, or larger areas formed by the coalescence of these, and is usually associated with acute or chronic pancreatitis, tumour-formation, obstruction of ducts, injury to ducts, etc. **Microscopically,** the areas are more or less homogeneous in appearance, and do not stain with osmic acid—the fat having become disintegrated, and probably converted into a compound of a fatty acid united with a calcium base. The pathology of this condition is referred to in Chapter III, p. 99.

ATROPHY of the pancreas occurs in old age and in wasting diseases; and, in these cases, is usually general throughout the gland. Localised atrophy may result from pressure, or from obstruction of the ducts. In some cases of diabetes mellitus, the pancreas is atrophied; and, in carcinoma and in cirrhosis of the gland, there may be very marked atrophy of the secreting tissue. In cases of interstitial pancreatitis, the atrophy of the organ may be extreme.

[1] Beattie, "Hæmochromatosis with Diabetes Mellitus," *Jour. Path. and Bact.,* Edinburgh and London, August 1903, p. 117.

INFLAMMATION OF THE PANCREAS :--

Inflammation of the pancreas may be acute or chronic, and affects the glandular or the interstitial tissue. According to the statements of Mayo Robson and Cammidge,[1] the condition of pancreatitis, especially the interstitial variety, is much commoner than is generally recognised; and they attribute to this disease of the pancreas many of the symptoms which are commonly regarded as being associated with gall-stones.

The forms of pancreatitis usually described are--

1. **ACUTE HÆMORRHAGIC PANCREATITIS**—to which sufficient reference has already been made.

2. **ACUTE SUPPURATIVE, GANGRENOUS, or NECROTIC PANCREATITIS** –though it may result as an extension of septic processes in the neighbourhood, as, for example, from a gastric or duodenal ulcer —is sometimes **primary,** the infection coming apparently from the intestinal tract by way of the ducts. It has been shown experimentally that injection of substances such as sulphuric and nitric acid, artificial gastric juice, and suspensions of various organisms, into the gland-substance, directly or through the ducts, may give rise to necrotic, hæmorrhagic, and suppurative conditions. The pancreas, in any of these conditions, is swollen and extremely soft, and shews a varying number of necrotic foci or gangrenous cavities.

3. **CHRONIC INTERSTITIAL PANCREATITIS.**—Mayo Robson [2] has divided this chronic form as follows :—

i. **Interstitial Pancreatitis :** –

(*a*) **Inter-lobular.**—In this, the inflammatory process is localised at the periphery of the lobules; and the cellular structure, with the islets of Langerhans, is affected only in the later stages.

(*b*) **Inter-acinar.**—The new fibrous tissue is diffusely distributed and invades the lobules, separating the individual acini, and invading the islets of Langerhans.

ii. **Cirrhosis of the Pancreas,** is a combination of inter-lobular and inter-acinar changes, with very great overgrowth of fibrous tissue.

In all the forms of interstitial pancreatitis, the pancreas, in the early stages, is hard and enlarged. On section, the amount of interstitial tissue is greatly increased. In the later stages, there is atrophy of the organ, and, on section, very little of the glandular elements of the pancreas can be detected. **Microscopically,** the cells are atrophied or degenerated, and there is marked overgrowth of fibrous tissue, which may be cellular, but, more commonly, is dense, fully-formed tissue. In some cases, the interstitial overgrowth may be so great that almost the whole of the secreting cells of the organ are destroyed. The islets of Langerhans may or may not

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[1] Mayo Robson and Cammidge, *The Pancreas : Its Surgery and Pathology,* W. B. Saunders Company, Philadelphia and London, 1907.

[2] Mayo Robson, *Brit. Med. Jour.*, 1904, vol. i. pp. 659, 719, 773. Mayo Robson and Cammidge, *The Pancreas : Its Surgery and Pathology,* W. B. Saunders Company, Philadelphia and London, 1907.

be involved in the process; and it has been suggested that the glycosuria which is frequently associated with interstitial pancreatitis may be caused by the involvement of these islets. There is, indeed, evidence that the pancreas produces an internal secretion which serves to maintain carbohydrate metabolism in a normal condition, and, in all probability, this secretion is produced by its islet-tissue.

Localised areas of interstitial pancreatitis may occur. Thus, Lancereaux [1] described a case in which the middle third of the pancreas was merely a fibrous cord, and the left lateral third much atrophied. This condition was associated with diabetes mellitus.

Ætiology of Interstitial Pancreatitis.—As already stated, it may be a sequel of the more acute processes, but, in most cases, the condition is either subacute or chronic from the beginning. Obstruction of the pancreatic duct by pressure from without, or by foreign bodies, catarrhal processes, tumours, calculi, etc., from within, may give rise to interstitial changes in the organ. Thus, it sometimes arises as a result of gall-stones blocking the common outlet, pancreatic calculi, tumours, or catarrh of the duodenum. Toxic products, of known or unknown nature, must be regarded as important causal factors. Thus, cases have been recorded which seem to have arisen secondarily to alcoholism, syphilis, purulent peritonitis, typhoid fever, influenza, mumps, etc. These toxic agents possibly act by producing gastro-duodenal catarrh, which spreads up the pancreatic duct. It has been shewn experimentally, by the injection of oil of turpentine, alcohol, agar, and other foreign bodies, into the pancreatic duct, that sclerosis of the gland may be produced. In many cases, the cirrhosis of the pancreas is associated with cirrhosis of the liver.

GRANULOMATA :—

TUBERCULOSIS OF THE PANCREAS is rare. Miliary or solitary nodules are sometimes seen, and the organ may be involved from neighbouring tuberculous glands.

SYPHILIS may give rise, as has been stated, to interstitial pancreatitis, and involvement of the pancreas is commonest in the congenital form of the disease. It is frequently associated with interstitial overgrowth in other organs, as, for example, in the liver and in the lungs.

TUMOURS AND CYSTS :—

Sarcoma is said to occur both as a primary and as a secondary growth, but it must be extremely rare.

Primary Carcinoma of the **scirrhus, encephaloid,** or **colloid type,** is said to occur in the head of the pancreas with comparative frequency. All the cases we have seen, some of which have been described as primary cancers of the head of the organ, have been tumours which have started apparently in the glands of the neighbourhood, and secondarily invaded the

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[1] Lancereaux, *Bull. Acad. de Med.*, Paris, 1877, series 2, tome vi., p. 588.

pancreas; and therefore we are somewhat doubtful about the comparative frequency of primary tumours of this organ. **Secondary invasion** of the pancreas by cancers of the stomach or liver, is, however, not uncommon.

Cysts of various kinds may occur :—

(1) **Congenital cystic disease,** associated with cystic kidney, and sometimes also with a similar condition in the liver, has been observed.

(2) **Retention-cysts,** due to obstruction of the pancreatic duct by calculi, cicatricial stenosis, pressure from without, or its involvement by malignant tumour of the head of the pancreas, or of the pylorus or duodenum, may occur. In a case seen recently by one of the authors, a very large retention-cyst in the tail of the pancreas simulated, and was, before operation, taken to be, a considerably enlarged spleen.

(3) **Hydatid cysts** are extremely rare, as are also cysts which result from the **absorption of hæmorrhage** or **of the products of necrosis.**

DIABETES MELLITUS

The pathology of this disease is still obscure, but, in a certain proportion of cases, the condition seems to be definitely related to disease of the pancreas. Lancereaux,[1] in 1877, pointed out the intimate association of **glycosuria** with profound alterations in the structure of the pancreas, but it was the experiments of Minkowski which firmly established the connection between the two conditions. He shewed that **total extirpation** of the pancreas in dogs gave rise to a condition strictly comparable to diabetes mellitus in the human subject. Clinical and *post-mortem* experience has given strong support to these experimental results. Various observers have shewn that extensive disease of the pancreas is frequently accompanied by diabetes mellitus. **Atrophy,** as a result of the impaction of calculi in the pancreatic ducts, or of obstruction of the latter by the pressure of calculi in the bile-passages : **interstitial inflammation,** however produced : **necrosis: so-called hyaline degeneration** of the parenchyma, etc., are all causal factors in certain cases.

Though the pathological lesions found in the pancreas in cases of diabetes are never so severe as to throw the organ out of use, as is necessarily done in extirpation of the gland or even in ligature of the duct, yet there seems little doubt that the glycosuria in diabetes is due to disease in the pancreas. It has already been pointed out that the islands of Langerhans have no direct anatomical connection with the pancreatic ducts. Further, these isolated groups of cells are scattered widely throughout the organ and have a very rich blood-supply, their cells have a different form and arrangement from those lining the acini, and their protoplasm contains finer granules.

Opie and others consider it very probable that these islands are

[1]*Loc. cit.*

concerned in carbohydrate-metabolism, and regard them as structures producing an internal secretion which is liberated into the blood. Various observers have found extensive degenerative changes, especially of a hyaline nature, in the islands of Langerhans in cases of glycosuria. At the same time, this is not a constant finding, and, at present, it cannot be stated definitely that destruction of the islands of Langerhans is the sole cause of diabetes mellitus. If these islands are concerned with internal secretion, and if this secretion plays an important part in carbohydrate-metabolism, it may be that changes extra-pancreatic may cause interference with, or perversion of, that secretion. The relation, however, of disease of the pancreas to glycosuria is not very clear, but physiological research has thrown much light on the subject. It may be stated generally, that the monosaccharides glucose (or dextrose), maltose, and levulose, can be consumed by the tissues of the body, but that starch and allied substances, as well as cane-sugar, must first be hydrolysed by the action of ferments in the alimentary tract. One of these hydrolysing agents is the diastatic ferment of the pancreas. Eventually, the polysaccharides are converted into glucose, and this is carried to the liver by way of the portal vein, and, in the liver, becomes glycogen. This glycogen is set free from the liver and poured into the blood as dextrose. The conversion of the glycogen into glucose takes place by various stages and is effected by ferments, of which glycogenase, which is found in all the organs, is one of the most important. If the pancreas is removed, or if its ferments, which are necessary to this complete carbohydrate-metabolism, are altered or destroyed by disease, then the chain of events is broken. When the sugar reaches the liver, it has not been acted upon by the amylolytic ferments of the pancreas, and is in such a form that it is either not stored as glycogen, or is in such an unstable condition that the glycogenase is able to act so energetically that it decomposes at once all the pre-existing glycogen in the liver as well as any that may be in process of formation. Thus, excess of glucose is poured into the blood and much is excreted by the kidneys, but none, or very little, is oxidised in the muscles. There are, however, factors, other than these hypothetical ferments, which undoubtedly play some part in the production of glycosuria. Thus, it can hardly be questioned that glycosuria, in some cases, is profoundly influenced by the nervous system, especially the sympathetic system. It has been shown experimentally that stimulation of the splanchnic nerves causes glycosuria, if the adrenal glands are healthy. If these glands are removed, glycosuria does not occur. Again, stimulation of the adrenals, or injections of adrenalin, may cause glycosuria. Further, excess of thyroid secretion may give rise to glycosuria; whilst, in the absence of the thyroid, the production of glycosuria is very difficult (*see* Chapter on **Ductless Glands,** p. 834). Enough has been said to show that glycosuria alone may result from various factors, and, at present, it is not possible to estimate the share each of these may take in its production. Again, glycosuria itself is not the only factor

in diabetes in fact, it may occur as a symptom of other diseases. There are important alterations in protein- and fat-metabolism. Certain of the elements, which go to the building-up of proteins, *e. g.* some of the amino-acids, are more capable than others of being converted into sugars. It has also been shewn that, in the absence of the proper utilisation of carbohyrates, there is an imperfect oxidation of fats; and certain of the intermediate products, *e. g.* acetone, di-acetic acid, etc., may appear in the urine.

Lipæmia—the presence of fat shewing on naked-eye examination in the blood and giving the serum milky appearance—is not uncommon in diabetes. The precise origin of this fat, and the reason for its accumulation in the blood, is not known.

Thus, it may be said that the diabetic condition is an abnormal metabolism of the carbohydrates, the proteins and the fats; that this is, in part, due to abnormalities in the pancreatic secretion brought about in various ways, and especially by pathological conditions in the islands of Langerhans; but that there are definite associations, the nature of which is at present unknown, with changes in the nervous system, the adrenals, the thyroid, and possibly other of the organs of internal secretion.

Interesting and important though the whole subject of diabetes mellitus and of pancreatic disease is, the relation between the two conditions has not been established with sufficient clearness to justify further reference to it here.

DISEASES OF THE DUCTLESS GLANDS

THE ENDOCRINE ORGANS

(THYROID, THYMUS, PITUITARY, SUPRARENAL, PINEAL, etc.)

THESE are structures which are composed of secreting glandular tissue, the secretion of which is not carried away by a duct as in the case, say, of the pancreas or salivary glands, but reaches the circulation by way of blood-vessels or lymphatics. In addition to certain, as yet little understood, activities, the majority of these ductless glands--by means of their so-called **internal secretions** or **autacoids** (αὐτός, self, and ἄκος, a medicinal agent or remedy)— possess extremely important influences upon general metabolism and nutrition, and upon blood-pressure. Some of these autacoids act by stimulating or exciting cell-function and are called **Hormones** (ὁρμάω, I stir up). Others produce depression or cessation of function, e. g. placental extract inhibits the secretion of the mammary gland, and are therefore called by Schäfer **Chalones** (χαλάω, I make slack). They are not inactivated by boiling, and are of simpler chemical constitution than enzymes. In some diseases, certain of the glands producing such internal secretions may be affected **alone**; but, in other instances, important alterations may be found in **several**, or even in **all,** of them **simultaneously,** and may therefore be regarded as **diseases of a group,** rather than of a single gland. The **sexual glands** and **other organs** (Testis, Ovary, Uterus, Breast and Placenta), in addition to their primary functions, also produce internal secretions which influence general metabolism and nutrition. The alimentary mucous membrane and the pancreas, in addition to their other activities, possess endocrine functions, and interna secretions are also now commonly ascribed to the spleen, lymphatic glands bone-marrow, etc.[1]

DISEASES OF THE THYROID GLAND

(INCLUDING THE PARATHYROIDS)

Outline of the Physiology and Histology of the Thyroid.—The most impor ant function of the gland is the production of an **internal secretion** whic has a very important influence upon the growth and maintenance of the gener nutrition of the body-tissues, and upon general metabolism, especial upon that of calcium salts: upon blood-pressure, its action being mainly vaso-dilator one, influencing especially the peripheral circulation, its functio in this connection being closely associated with the sympathetic adrer system: and its secretion is also believed by some to possess importa functions in relation to the neutralisation and elimination of various toxins

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[1] Consult Schäfer's *The Endocrine Organs,* Swale Vincent's *Internal Secret: and the Ductless Glands,* Gley's *Les Sécrétions internes,* etc.

The gland is relatively larger in women than in men. It undergoes more rapid enlargement at **puberty,** and temporary alterations in its size are common, for example, enlargement at the menstrual periods and during pregnancy. It becomes relatively atrophied in old age.

The human thyroid is composed of a **lateral lobe** on each side, joined by the **isthmus.** The latter varies greatly in size in different individuals, and may, in some cases, be absent—a condition which is normal in certain animals, e. g. the sheep, in which the thyroid is therefore a paired organ. **Prolongations** of the glandular substance may be found passing upwards—or more rarely downwards—usually from the isthmus near the middle line. **Development-ally,** the thyroid arises from three independent rudiments—paired **lateral rudiments,** one on each side, which originate from the pharyngeal hypoblast of the fourth visceral cleft, and a **median rudiment** in the form of a divertic-ulum from the ventral wall of the pharynx. The last grows downwards,
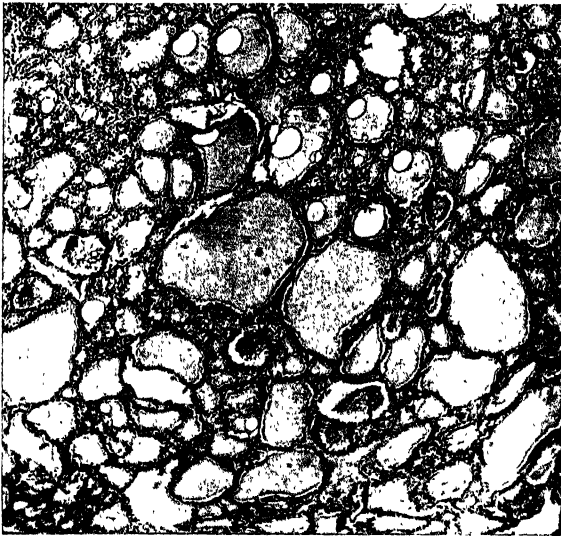
FIG. 377.—Section of Normal Thyroid. × 50.

and its lower end bifurcates to join the two lateral rudiments. This divertic-ulum at first possesses **a lumen,** passing from the foramen cæcum at the root of the tongue above, to the isthmus below, and constitutes the **thyro-glossal duct,** which, under normal circumstances, soon becomes obliterated and forms a fibrous cord. In rare instances, portions, or even the whole, of this duct may remain patent, and, occasionally, cyst-adenomatous, and other tumours arise from it.

Structure of the Thyroid Gland.—The organ is covered by a thin, dense, fibrous **capsule,** prolongations of which pass in as septa, dividing the gland into lobules, and containing blood-vessels and abundant lymphatics. The **blood-supply** of the gland is very large in proportion to the size of the organ; and the amount varies with its activity. **On microscopical section,** the glandular tissue is seen to be composed of **cyst-like spaces**—the largest of which may be just visible to the naked eye. They are lined by **low columnar, cubical,** or, in inactive glands, by comparatively **flattened epithelium;** and are filled with " **colloid** " material (see fig. 377). These cyst-like spaces are

sections of minute closed **vesicles**; but, early in development, the thyroid is a compound tubular or racemose gland, with acini and a duct—the **thyroglossal duct**— the developmental origin of which structure has already been described. This duct, as previously noted, normally undergoes obliteration, the tubular acini becoming converted into the closed, cyst-like spaces; but, in some pathological conditions, there seems to be a capacity of reverting to the structure of a racemose secreting gland; and an imperfect acinus-like grouping of the glandular cells around obliterated, and even partially patent, duct-like structures may be observed.

The Secretion of the Thyroid Gland. The **colloid,** or **mucoid,** material in the cyst-like spaces is not the essential element of the secretion, but is to be regarded rather as a **by-product,** such as may be derived from the activity of cells in any closed space. Similar colloid material is seen, not only in the thyroid itself, but also in certain parts of the pituitary and prostate glands, and also in the tubules of such glands as the kidney, when these become blocked from any cause. The production of this substance is due to changes in the lining epithelial cells, which, during the process, become much swollen, and contain droplets of colloid. The cells may either remain attached, or, more commonly, may be separated from the walls of the space, and undergo degeneration, their contents gradually fusing with the colloid pass in the space. The essential or true thyroid secretion is probably a fluid which permeates, or is contained in, this practically inert colloid material, in the same way as, say, strychnine or codeine may be dissolved and stored in a jelly, or as nutrient fluids are contained in gelatinised culture-media,-- *i. e.* the active substances secreted by the thyroid gland are only temporarily stored in this substance until they are required. They may then pass out by way of the lymphatics, or possibly directly by the blood-stream. These active substances may be extracted from the colloid artificially, and are not destroyed by drying or cooking the gland. It is preferable to adopt the term **Thyrine** for these substances, as suggested by Schäfer, rather than the older terms " Iodothyrin " or " Iodo-thyro-globulin," as their true nature is still unknown- although their activity is usually said to be parallel with the amount of combined Iodine contained in them. Their action is complex, being **hormonic** or excitory on some tissues, for example in connection with the sympathetic nervous system (either direct or through the intermediary excitation of the suprarenals), and also on the sexual organs, thymus, etc., though it is not yet known whether the action on these is direct or indirect; but **chalonic** or inhibitory on others, for example on the pituitary. Though the influence of the thyroid secretion affects practically every organ and tissue of the body, it is only known to be *specifically* connected with the **generative organs,** the **liver** and **pancreas** (in the assimilation of sugar and glycogen-production, the pancreas and thyroid having a mutual chalonic or restraining action the one on the other), with the **suprarenal medulla** and **sympathetic system** in general, and with the **pituitary** and **thymus glands.** The view that the thyroid secretion is concerned in the destruction of toxic substances circulating in the blood is, according to Schäfer, no longer tenable.

In some conditions in which the thyroid becomes **more actively secreting,** the colloid may partially, or even entirely, disappear; whilst, on the other hand, in conditions where the gland is **less active,** it may be greatly increased in amount. In some pathological conditions, especially in certain acute infective diseases such as pneumonia, septicæmia, etc., the secretion may become mucinoid and thin, the cells exhibiting active proliferative and catarrhal changes.

CONGENITAL ABNORMALITIES OF THE THYROID GLAND.—

Congenital Athyrea, or **Sporadic Cretinism,** due to absence of the gland, is discussed later, on p. 842.

Accessory Thyroids are by no means uncommon. They are usually small in size, and are generally found in the immediate neighbourhood of the main gland. They must be distinguished from the **parathyroid glands**—small structures, two of which lie on each side in close relationship to the lateral lobes of the thyroid, within the substance of which, in some animals, they may, indeed, be embedded.

ATROPHY.—**Senile Atrophy** occurs, the condition being not infrequent in elderly females who have suffered from enlargement of the gland during middle life. The fibrous tissue of the septa and the stroma, especially around the vessels, is increased in amount. The vesicles may undergo enlargement, the epithelial cells becoming flattened —*i. e.* there is less secreting structure and there is accumulation of passive colloid material. The more serious form of atrophy, leading to the production of **Myxœdema,** is discussed on p. 843.

WAXY or AMYLOID DEGENERATION is rare, but is occasionally found. It occurs under the usual conditions, and shews the usual characters of the disease elsewhere (*see* p. 53).

CLOUDY SWELLING is of frequent occurrence in **acute fevers** and **septicæmias,** and, as mentioned above, is often accompanied by replacement of the colloid by **mucoid** material, and by a **catarrhal** condition of the epithelial cells. These changes may become so pronounced as, in some cases, to constitute an **acute inflammatory thyroiditis.**

ABSCESSES.— Minute secondary abscesses may occur in **pyæmia** and in **ulcerative endocarditis.** They appear to be found especially in **staphylococcal infections.** Abscesses of larger size are rare.

TUBERCULOSIS.—A few small scattered granulations are usually found in cases of generalised **miliary tuberculosis. Larger tuberculous nodules** are occasionally met with in children.

SYPHILIS. —Actual gummata are very rare, the most important change produced in the gland by this disease being an **interstitial cirrhotic overgrowth,** especially in congenital cases.

ENLARGEMENTS AND TUMOURS

ENLARGEMENTS, or GOÎTRES.— These are due probably, in most cases, to some long-continued demand on the activity of the gland, possibly **toxic** in origin. According to some recent writers, in certain cases of thyroid enlargement, some septic focus may exist somewhere in the body, *e.g.* in the tonsils, nasal sinuses, teeth, etc., and the case may benefit from removal of such source of infection. Whether such benefit is due to the removal of the actual exciting cause, or merely to improvement of the patient's general health, is still an unsettled problem. In certain localities, *e. g.* in Gippsland, Australia, **insufficiency of lime** in the food and

water appear to be the chief causal factor of the mild thyrotoxic symptoms prevalent, these disappearing on the administration of calcium-salts. In some limestone hill-districts, *e. g.* Derbyshire—where the so-called "Derbyshire neck" is prevalent—Switzerland and elsewhere, on the other hand, **excess of lime-salts** leads to a non-thyrotoxic hypertrophy of the thyroid and parathyroids, which glands, as above stated, specially control calcium-metabolism. A hereditary liability, or transmission from parent to offspring, appears to play a part in some cases. The condition is found occasionally in some of the lower animals, for example in dogs, where such transmission from the mother appears to be not uncommon.

Simple Goître is essentially a **cystic** enlargement of the gland, the

Fig. 378.—*Cystic Goître.*[1]   Contrast with figs. 377 and 381.   × 50.

cysts varying greatly in size. They may be very numerous and be distributed uniformly throughout the enlarged organ (*see* fig. 378); or they may occur in localised areas. They contain colloid material, and sometimes altered blood. Papillary ingrowths are common. In other cases, the overgrowth may be largely **fibrous,** usually with an admixture of cysts. Occasionally, a **simple hyperplasia** is found, in which the histological appearances are apparently those of normal thyroid tissue.

These varieties of goître are, as a rule, not serious in their results, except from the inconvenience of their size—which may be very considerable—or, in some cases, on account of **pressure-results,** *e. g.* upon the trachea or œsophagus. Secretion does not appear to be specially

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[1] The retraction of the contents from the walls of the spaces in this specimen is an artefact produced during its preparation.

interfered with, except in rare cases, where it may become deficient, a condition which may ultimately lead to results resembling those seen in sporadic Cretinism or in Myxœdema (*q. v.* pp. 842 and 843).

EXOPHTHALMIC GOÎTRE.—(Described by Parry in 1825, and by Basedow in 1840, and often associated with their names. The condition is also frequently referred to as Graves' Disease.) This disease is characterised by (1) **enlargement of the thyroid,** with definite and very typical pathological alterations, which are often accompanied by changes in other glands and tissues, especially in the **thymus;** (2) **tachycardia** or acceleration of the heart's action, usually accompanied by cardiac irregularity; (3) **lowered arterial tension,** due to dilatation of the blood-vessels, and especially noticeable in the vessels of the face and neck; (4) **exophthalmos** or protrusion of the eyeballs, with enlargement of the palpebral opening; (5) **fine muscular tremor, nervous excitement, palpitation,** etc.; (6) **changes in nutrition,** wasting and emaciation, raised temperature, abnormalities in pigmentation, sometimes polyuria without sugar (in 13·5 per cent. of cases), alimentary or transitory glycosuria (permanent only in 2 per cent.), and albuminuria in about 11 per cent.; (7) **blood-changes,** usually of the nature of an anæmia, accompanied, in many cases, by profound alterations in the bone-marrow.

The disease is much commoner in women than in men, although an increased proportion of cases of thyroid enlargement, with many of the symptoms of exophthalmic goître, appears to have occurred among soldiers during the recent war. The disease supervenes usually about the third decade of life. It varies considerably in duration—acute, subacute, and chronic types being recognisable. Cases of recovery are recorded, aided, it may be, by suitable treatment, X-ray administration, etc.—otherwise the disease is usually progressive, though perhaps with intermissions. In **acute** cases, death may supervene in a few months, or perhaps weeks, and, in several recorded cases, even within a few days of the onset of the symptoms; whilst the more **chronic** cases may last for several·years, and may shew intermissions and relapses.

In this disease, a **constant pathological change, unlike that found in any other disease of the gland, is present in the thyroid;** and the symptoms, as has been pointed out by Moebius on the Continent, and by Greenfield in this country, appear to be due to an accompanying **increase,** and perhaps also **perversion, of the thyroid secretion,** *i. e.* a condition of **hyperthyrea** or **hyperthyroidism.** Most of the symptoms—even the exophthalmos—may be artificially produced by overdoses of the extract of the normal gland; and, moreover, the disease forms a striking contrast with myxœdema, a condition which is due to insufficiency of the gland (*see* p. 843), and which may, therefore, in some ways be regarded as its antithesis. In a few cases in which secondary atrophic changes occur in the enlarged thyroid, **myxœdema** may·supervene upon the primary condition of exophthalmic goître.

Changes in the Thyroid itself.—There is usually marked, and, in some cases, very considerable, enlargement, involving all parts of the gland, although sometimes slightly asymmetrically, the right lateral lobe frequently shewing distinctly greater increase than the left. The gland usually retains more or less its normal shape, but the lateral lobes have a

FIG. 379.—*Thyroid Gland, etc.* From a case of Exophthalmic Goître.

1. Hyoid bone. 2. Thyroid cartilage. 3, 4, 5. Central, left and right lobes of enlarged thyroid gland. 6, 6, 6. Greatly enlarged thymus gland. 7. Pericardium. 8, 9. Right and left ventricles of heart. (From a specimen lent by the late Professor Greenfield.)

marked tendency to enlarge backwards, and may come almost to surround the trachea and even the œsophagus, and perhaps almost meet behind these structures and cause their compression. The enlargement in exophthalmic goître is, however, as a general rule, not so great as in many cystic goîtres. In colour, the gland is usually very **pale,** and, as has been pointed out by Greenfield, it closely resembles, on section, an

actively secreting salivary gland, or the pancreas, in general naked-eye appearance. Though usually moderately firm and elastic, it is distinctly softer than the normal gland in consistence, and exhibits more lobulation,

Fig. 380.—*Thyroid Gland, etc.* From a case of Exophthalmic Goitre (seen from behind).

1. Tongue. 2, 2. Œsophagus (into which a glass rod has been inserted). 3, 4. Lateral lobes of enlarged thyroid gland. 5. Aortic arch. (From a specimen lent by the late Professor Greenfield.)

the surface occasionally presenting slight nodulation. Cysts are not common, and, if they do occur, are usually small, and have fluid—not colloid —contents. The surface veins may show marked engorgement, and the vascularity of the glandular tissue itself resembles that of any other actively functioning gland. According to Greenfield, the enlargement of the

gland is thus not due to vascular dilatation, as was previously believed by many—the " pulsation " which is often described being communicated from the neighbouring arteries at the root of the neck.　**On section,** the gland-tissue is pale pinkish-white in colour, and, as already noted, closely resembles that of an **actively secreting gland,** such as the pancreas or a salivary gland.　**On microscopical examination,** the tissue of the organ shews **enormous proliferation of the secreting structure,** comparable to the active proliferation seen in the functioning mammary gland during lactation.　The process is not a mere dilatation of the spaces, but an actual proliferation of the epithelium, which may shew papillary ingrowths into the spaces.　These become smaller in size, and are transformed into what
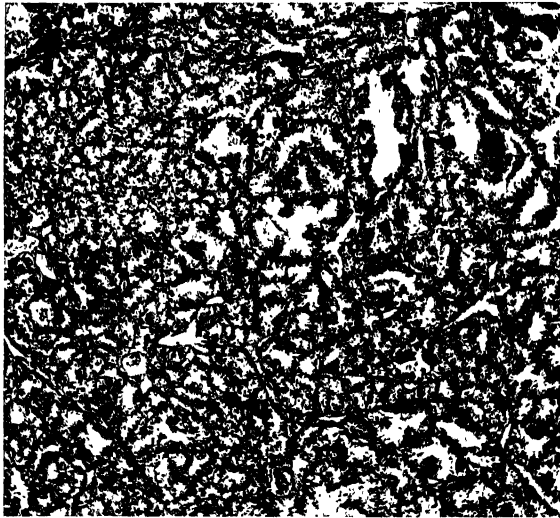
Fig. 381.— *Thyroid Gland* in Exophthalmic Goître, shewing the active proliferation of epithelium, disappearance of colloid, etc.　× 50.

closely resemble the tubular acini of a racemose gland.　The cells, instead of being more or less flattened, become cubical, or even columnar in shape, and may shew active mitosis, and catarrhal and degenerative changes.　The **colloid disappears,** and the contents of the acinus-like spaces become more fluid in consistence, and contain the débris of degenerating cells.

Associated Changes in Other Organs and Tissues.—The **lymphatic glands,** both in the immediate neighbourhood of the goître, and also in the mediastinum and abdomen, are often enlarged and unduly vascular. Enlargement of the **hæmolymph-glands** is also a frequent phenomenon, and has been observed in the majority of cases of exophthalmic goître examined by the authors during the past fifteen years.[1]

[1] For a detailed description of the enlarged hæmolymph-glands in a case of exophthalmic goître, *see* Lorrain Smith, " On a case of Hæmolymph Glands," *Medical Chronicle,* March 1908.

The **thymus gland,** in cases of exophthalmic goître, is very frequently persistent, and, in many instances, considerably enlarged (see fig. 379, 6, 6, 6). **On microscopical examination,** this enlargement of the thymus appears to be. of the nature of a simple hyperplasia.

The **spleen** is occasionally enlarged, and exhibits, as a rule, evidence of increased hæmolytic activity.

The **bone-marrow,** in a series of ten cases examined by one of the authors, was found to shew very marked changes, mostly of the nature of a mixed **leuco-** and **erythro-blastic** reaction. The fatty marrow of the long bones was usually completely transformed to red marrow; and, especially in several very acute cases examined, was dark brick-red in colour, resembling the naked-eye appearance seen in some cases of pernicious anæmia, when the latter is characterised by excessive pigmentation. The medullary cavity was enlarged, the osseous trabeculæ, and even much of the compact bone itself, being extensively absorbed. In these **acute** cases, the marrow, under the microscope, shewed advanced degenerative changes, generally of the nature of gelatinous degeneration, the previously proliferated hæmopoietic cells having undergone extensive atrophy, and the marrow exhibiting large numbers of actively phagocytic cells containing blood-cells and pigment. The occurrence of megaloblasts was not uncommon, and in five cases examined, the eosinophil cells in the marrow shewed distinct increase in number.[1] These changes point to the action of some actively toxic agent, which at first produces a leucoblastic reaction : and later, as anæmia is established, a supervening erythroblastic change. The marrow then becomes exhausted, and undergoes the degenerative change above noted. In the more **chronic** cases, similar, but, as a rule, less pronounced, changes were found.

The clinical examination of the **blood** gives, in many cases, very little indication of the marked marrow-changes present. Most authors who deal with the blood-condition note the occurrence of a mild, or occasionally severe, anæmia, " chlorotic in type," sometimes with relative lymphocytosis.[2] The eosinophils may be increased in some cases.

The **peri-** and **endo-cardium** are often affected, but whether from the direct action upon them of the altered and increased thyroid secretion, or by its indirect action rendering them more liable to acute rheumatism, has not yet been determined. Death, in these cases, is not infreqently due to **pericarditis;** and **endocarditis** is also by no means uncommon. The **simultaneous occurrence of mitral and tricuspid stenosis** in several cases of exophthalmic goître has been noted by Greenfield.

Degenerative changes in the nervous system have also been described,

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[1] Carnegie Dickson, The Bone-Marrow, Longmans, Green & Co., London, 1908, pp. 62 and 51.
[2] Ewing, Clinical Pathology of the Blood, Kimpton, London, 1904, p. 387; and Cabot, Clinical Examination of the Blood, Longmans, Green & Co., London, 1904.

e. g. in the cervical and other ganglia of the sympathetic system, and also in the medulla. Bruce and Pirie have described degenerative lesions in the **intermedio-lateral tract** of spinal nerve-cells in the upper dorsal region, which they associate with the abnormalities of sweating frequently observed in this disease.

ATHYREA and HYPOTHYROIDISM.—Partial or **complete absence** of thyroid secretion leads to extremely important changes in the nutrition of the tissues, and may be discussed under three types :—

1. **Congenital Athyrea, or Cretinism.**
2. **Operative Athyrea,** or the **experimental** or **therapeutic removal of the gland,** in whole or in part.
3. **Degenerative Athyrea, or Myxœdema.**

1. **CONGENITAL ATHYREA, or CRETINISM.**—In this and allied conditions, the thyroid gland is either entirely absent, or has undergone early, and perhaps complete, atrophy. The tissues of the infant are, therefore, deprived of the influence of its secretion during the period at which their growth should be most active. As a result, the **cretin** is stunted both in body and in mind, *i. e.* the condition is one of **defective development with idiocy,** the central nervous system, bones, connective tissues, and skin, being especially affected. The skin is lax, dry, and harsh, the hair scanty, and dentition delayed and imperfect. Pads of redundant subcutaneous fat are usually present, especially above the clavicles. The tongue is large and may be protruding, the abdomen is prominent, and the limbs are stunted in their growth.

Cretinism may be **sporadic,** associated with absence or early atrophy of the thyroid: or **endemic,** usually due to goîtrous degeneration. The latter type is again subdivided into the **myxœdematous,** in which the parathyroids survive, the commonest type in Europe, and the **nervous,** in which they are also involved. Heredity, or family predisposition to the disease, has been observed in some instances. The symptoms of congenital cretinism, even with complete athyrea, may not shew until some little time after birth. Cretins are specially liable to be attacked by infective disease, the symptoms of which may be masked, sometimes to an extraordinary extent. Thus, in one case examined by Carnegie Dickson, a cretin child, sitting up in bed playing with its toys and not shewing any symptoms unusual to it, suddenly fell back dead, and was found on *post-mortem* examination to have well-marked tuberculous meningitis, of which, during life, it shewed no symptoms obvious. In like manner, the symptoms of other forms of meningitis, as well as of pneumonia, general tuberculosis, etc., may be masked in cretins.

Occasionally, a similar condition of athyrea may supervene in previously healthy children, *e. g.* about the age of four or five. This has been termed **juvenile myxœdema,** and is due to atrophy of the thyroid gland, perhaps after an attack of some acute infective fever.

2. **OPERATIVE ATHYREA.**—Unless the secretion of the thyroid has previously become diminished or much modified by disease, the complete removal of the gland produces very acute symptoms, though these depend, to a considerable extent, on the species of the animal and its age, young animals being much more susceptible. Thus, **experimental thyroidectomy** in animals, e. g. cats or monkeys, leads to **acute nervous symptoms,** such as convulsions, tetany, etc.; and apathy, coma, and death may supervene in the course of a few days or weeks. These symptoms are due, in part, to the concurrent removal of the **parathyroid glands,** and, if these are left, the symptoms are much less severe, and tetany does not necessarily supervene. If such animals, e.g. the monkeys, be kept warm, they may survive the immediate effects of removal, and may develop typical symptoms of **myxœdema** (Forsley). **Thyroidectomy**
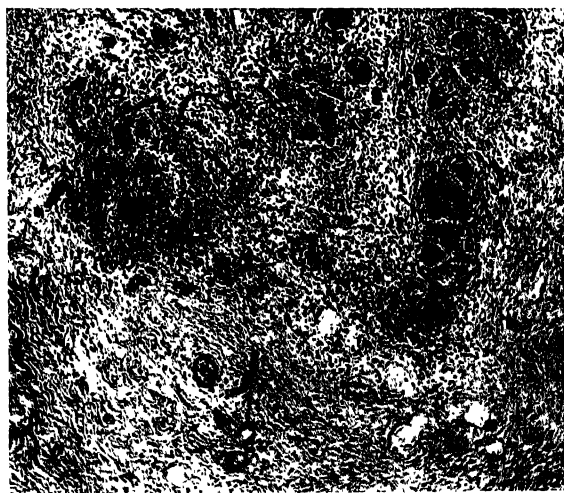
Fig. 382.—*Section of Thyroid Gland.* From a case of Myxœdema, shewing atrophy of the glandular tissue, with fibrosis, and collections of small round cells around duct-like structures.   × 50.

in the human subject has frequently been performed for tumour of the gland and in cases of exophthalmic goître, the subsequent history of such cases varying greatly. Even a small piece of the gland left behind at such operation may avert the acute phenomena already described as occurring in the lower animals, but, in some cases so treated, these have supervened.

3. **DEGENERATIVE ATHYREA, or MYXŒDEMA.**—Although **acute** forms of this disease occur, the condition is much more commonly a **chronic** one in character. It is a slow and progressive **atrophy of the gland**—often more marked upon the right side—followed by secondary changes in the various tissues of the body. The thyroid itself may be reduced to a mere mass of fibrous tissue, all the glandular structure having disappeared. The degenerative changes, in some cases, begin

by an invasion of the stroma with numerous small round cells, which produce an appearance like that of an adenoid tissue. In other cases, nothing may be found except structures resembling the remains of ducts, scattered amongst fibrous tissue, no glandular cells surviving (see fig. 382).

These changes may come on insidiously and with no, as yet ascertainable, cause; but, in some instances, they follow certain other conditions of the gland, e.g. **exophthalmic goître.** In such cases, the degenerative changes supervene upon a previous enlargement and increased activity. These cases, therefore, often present a varying symptom-complex allied to both conditions. A similar atrophy of the gland, with development of myxœdematous symptoms, sometimes supervenes in cases of exophthalmic goître in which the thyroid has been exposed to an excessive course of X-ray treatment.

Myxœdema occurs much more frequently in females than in males, the proportion given by Osler being 6 : 1. A predisposition, or increased liability, to disease of the thyroid gland, may, in some cases, be observed among members of the same family, and numerous instances in which cases of myxœdema and of exophthalmic goître have thus occurred are recorded.

Secondary Changes in the Other Organs and Tissues in Myxœdema. The skin and subcutaneous tissues are specially affected. The skin is dry and pale, and often presents a somewhat yellowish tint. There is atrophy of the sweat- and sebaceous glands and hair-follicles, the hair becoming coarse and scanty. There is accumulation of gelatinous-looking material in the subcutaneous tissues—probably a mucoid degeneration of the connective tissue (see p. 51) —due to interference with both the formative and the absorptive processes normally occurring in the tissues. Similar changes take place in the **lips, tongue,** etc., and the features have a puffy, bloated appearance, which may, at first sight, be mistaken for a symptom of Bright's disease. The fullness of the skin and subcutaneous tissue is, however, not due to mere œdema; it does not pit on pressure; and other differences, e.g. in distribution, may be noted. There is frequently a localised **malar flush;** and the **supraclavicular pads,** already noted as common in cretinism, are also usually present in myxœdema.

The **connective-tissue framework** of the various organs and tissues of the body may exhibit changes similar to those found in the subcutaneous tissue. The **peripheral nerves** may shew degeneration of their nerve-fibres, and there is, very commonly, an accompanying myxomatous change in their connective-tissue sheaths (see Chapter on **Nervous System,** p. 1017). Degenerative and atrophic changes are also found in the **central nervous system,** e. g. subacute general chromatolysis of nerve-cells (Brun and Mott).

Metabolic processes are sluggish, oxygen-intake and nitrogen-output are decreased; the body-temperature is lowered, there is increased

tolerance for sugar, and the sexual functions are diminished or in abeyance.

The most remarkable feature in cases of the various forms of athyrea is the rapid improvement, and perhaps, if not too long delayed, the complete disappearance of the symptoms of the disease, on the continuous administration of thyroid gland, either in the form of fresh or dried gland, or as an extract.

One point of importance, which has been specially emphasised by Greenfield, is the increased liability of myxœdematous patients to become the subjects of **tuberculosis,** which may run a very rapid, " latent " course, *i. e.* may give rise to little or no clinical evidence of its presence.

The **blood-condition** in myxœdema is usually one of progressive **anæmia,** secondary in type, and occasionally accompanied by slight leucocytosis. A few nucleated red cells may be found, and an increase in the size of the individual red cells has been described. The **bone-marrow,** in two cases examined by one of the authors, shewed very extensive mucoid or gelatinous degeneration, with great diminution in the number of the hæmopoietic cells. In one of these cases, which died of pneumonia, there was little or no leucoblastic reaction in the tissue.

DISEASES OF THE PARATHYROID GLANDS

The Parathyroids are two pairs of minute glands which, in man, are usually closely attached, one pair on each side, to the outer margins of the lateral lobes of the thyroid, the upper pair being frequently entirely embedded in the thyroid substance. Their functions are usually regarded as independent and distinct from those of the thyroid, as is also their developmental origin from the third and fourth visceral pouches, from which the thymus also is derived. Intermingling, or inclusion one within the other, of the elements of thyroid, parathyroids, and thymus occasionally occurs.

In structure, the Parathyroids consist of epithelial cells, sometimes compact, sometimes divided up into lobules by strands of connective tissue; and, occasionally, small vesicles containing colloid occur. These glands have a very abundant blood-supply.

If, in the lower animals, all the parathyroids are removed, death usually supervenes in a few days or weeks, paroxysms of clonic contraction of the muscles, exaggeration of the reflexes, gasping respiration and quickened pulse, being among the characteristic symptoms. In man, on the other hand, the muscular contractions tend to become tonic rather than clonic, associated with diminution of the respirations and of the frequency and force of the heart-beats, and fall of body-temperature. Total extirpation of the parathyroids is, therefore, associated with a form of " **tetany** " (*Tetania parathyreopriva*). This has been proved to be due to involvement of the lower neurones, and is relieved by injection of parathyroid extract, or by grafting the gland, the function of which, therefore, appears to be the production of an internal secretion or autacoid (presumably of a chalonic or restraining nature) which tends to prevent over-excitation or discharge of nerve-cells.[1] Noel Paton and his colleagues have shewn that the secretion of the parathyroids probably detoxicates or renders innocuous a poisonous substance of the nature of a guanidine-compound derived from muscular metabolism, the presence of which, if it is not removed, leads to the production of tetany.[2]

Clinically, various diseases or syndromes of symptoms have been attributed to changes in the parathyroids. **To atrophy or diminished secretion,** have been ascribed **the tetany of infants,** of **pregnancy** and of **various infective diseases :** and **to enlargement or increased activity** and **to altered secretion,** various **nervous diseases** such as myotonia paralytica and myasthenia gravis. The latter suggestion as yet lacks confirmation ; but the former is possibly supported by the finding of hæmorrhage or some other lesion in the glands of cases in which certain forms of tetany have been present, as described by some authors.

[1] Schäfer, *loc. cit.*, p. 24.
[2] *See* Halliburton, *British Medical Journal*, March 26, 1921, p. 450.

DISEASES OF THE THYMUS GLAND

This organ, with its two main lobes, subdivided into lobules, which consist of adenoid tissue arranged around the concentric Hassal's corpuscles, reaches its maximum development at or about the second or third year of life; and, after puberty, it normally undergoes gradual atrophy. In the adult, it is generally represented by a small bilateral pad of fatty tissue behind the manubrium sterni and overlapping the upper part of the pericardium anteriorly. The specific functions of the organ are still obscure. Experimental work by Noël Paton and others has proved a definite relationship between the thymus and the testes. In castrated cattle, the thymus remains about twice its normal size, and its involution is retarded. If both testes and thymus are removed in young guinea-pigs, their rate of growth is retarded, a result not produced by the removal of either alone.

Persistence of this gland after puberty is by no means uncommon, and, occasionally, the organ may shew distinct **hyperplasia.** The enlargement of the thymus in **lymphatism** has already been described (p. 647). In **exophthalmic goître,** the thymus is very frequently persistent, and often markedly enlarged (p. 841; and fig. 379). **Diminution in size** occurs rapidly in starvation and other forms of inanition.

Acute changes are not uncommon in this organ in children who have died of any of the acute infective diseases. **Hæmorrhages** may occur under similar conditions, and also in death from suffocation. **Abscess** of the thymus may be found; but **post-mortem softening** of the tissue, which not infrequently supervenes soon after death, should not be confused with true suppuration, the naked-eye appearances of which it may closely simulate. The organ is usually involved in anterior mediastinitis. **Tuberculous lesions,** and, less commonly, **syphilitic gummata,** occur.

Lymphomata and **lympho-sarcomata** may arise from the thymus.

DISEASES OF THE SUPRARENAL OR ADRENAL BODIES

Developmentally and physiologically, the suprarenal consists of two distinct portions, the **Cortex** and the **Medulla.** In man and other mammals, the medulla is completely enclosed within the cortex; but, in amphibia, reptiles, and birds, they merely interlock; whilst, in fishes, they remain as anatomically separate organs. The **cortex** is derived from mesoderm-cells of the genital ridge, and some of its functions are probably intimately connected with those of the sex-glands, and probably also with the elaboration of metabolic substances which are utilised by other organs and tissues. The **medulla,** on the other hand, is developed from the same series of neuroblast-cells which gives rise to the sympathetic ganglia, and this portion of the gland produces the extremely important internal secretion variously termed **Suprarenal Extract, Suprarenin, Adrenalin,** or **Epinephrine,** the chemical nature and physiological actions of which have been very extensively studied. It has been prepared synthetically (ortho-dioxyphenyl-ethanol-methylamine [1]), its most important actions being the **constriction of the majority of the peripheral arteries** (especially of the splanchnic area and skin, but not the coronary arteries of the heart), and the muscular coat of veins, **slowing of the heart-beat** (if the vagi are intact - otherwise there is acceleration) : its action on other **involuntary muscular tissue supplied by the sympathetic,** resulting, in some instances, in **increased contraction** (sphincters of the pylorus [2] and ileo-cæcal valve,[2] spleen, uterus, vagina, vas deferens, retractor penis, dilator pupillæ), but in **inhibition** in other cases (œsophagus, stomach, intestine, gall-bladder, urinary bladder). Other results are **increased flow of saliva and tears,** and of **mucous secretion** of the mouth, throat and trachea. It **defers muscular fatigue,** and has an important influence on **pigment-cells and pigment-production.** Its **local hæmostatic action** is well known and is now constantly used in surgery. Over-doses lead to **hyperglycæmia** and **glycosuria,** even with a carbohydrate-free diet, from its action on the liver and pancreas; and its **prolonged administration** leads to a form of **arterio-sclerosis** due to the long-continued high blood-pressure. The large blood-vessels near the heart, probably on account of the relatively small amount of muscular tissue in their walls, are not constricted, but rather undergo passive dilatation due to the increased blood-pressure.

In the human fœtus, the suprarenals are of relatively large size, owing to the greater development of the innermost part of the cortex next the medulla. This well-developed **boundary zone** does not show lipoid granules, but, after birth, the cells undergo fatty degeneration and disappear by about the end of the first year of extra-uterine life. At birth, the part of the cortex superficial to this boundary zone is narrow, but gradually enlarges to form the adult cortex, as the fœtal boundary zone atrophies.

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[1] Given as " orthodioxyphenylethylolmethylamine," by Macleod, who notes its close relationship to tyrosine and to a group of substances (amines) occurring in putrid. meat, and to which the active principles of ergot belong. The synthetic preparation, although in chemical composition apparently identical with the natural epinephrine, is comparatively inert, probably because it consists of a racemic mixture of lævo- and dextro- forms of the base. It may be rendered physiologically active by combining the racemic mixture with an optically active acid, fractionally crystallising the solution, and so isolating the lævo-form, the action of which on the organism appears to be that of the natural substance.

[2] Congenital Hypertrophic Stenosis of these sphincters is believed by some to be due to " hyper-adrenalism " (see pp. 747-8).

The course of the blood-flow in the suprarenal somewhat resembles that of the lymph in a lymphatic gland, the arteries being distributed to the periphery like the afferent lymphatics, and giving rise to a rich capillary plexus running between the columns of the zona glomerulosa and zona fasciculata. In the zona reticularis, these become large and sinus-like, and, from the latter, the blood passes directly into the venous sinuses of the medulla, from which it is collected into the single vein which leaves the hilus like the efferent lymphatic. For its size, the suprarenal has a more abundant blood-supply than any other organ or tissue in the body.

On naked-eye examination, the somewhat flattened, triangular bodies with rounded edges, present, **on section,** a radially striated, yellow-ochre-coloured cortex, the tint of which usually becomes darker as age advances. The medulla or central portion of the gland varies greatly in bulk, and is often opaque pearly-white in appearance, though in many cases it may, from the presence of pigment, present a dark-brownish tint. **On microscopical examination,** the **cortex** may usually be differentiated into three zones, the epithelial cells immediately beneath the capsule being arranged in thick, inter-communicating columns bent on themselves at the surface into narrow loops or arches with their convexity outwards. Towards the surface, sections of these columns or cell-groups form more or less rounded or oval masses, and this layer is therefore called the **zona glomerulosa.** When traced inwards, the columns become more regularly distributed into the narrower, radially arranged columns of the **zona fasciculata,** which constitutes the main bulk of the cortex. The deepest layer of the cortex—the **zona reticularis** — is formed of a meshwork of branching and anastomosing columns of cells which are usually rich in pigment. In the human subject, these various layers run gradually into one another. The cortical cells are extremely rich in fatty and lipoid substances. The **medulla,** or central portion of the gland, contains numerous thin-walled, dilated, venous-capillary spaces, into which the blood from the cortex directly flows. Between these lies a reticular stroma in which are embedded groups of polyhedral or irregular cells, which are clearer and more vacuolated than those of the cortex. They are arranged in irregularly anastomosing columns, surrounding large blood-sinuses which are continuous with those of the zona reticularis. " The Medulla is better described as a solid cell-mass permeated by sinus-like blood-vessels with the cells compactly arranged between and around them." [1] These cells are rich in granules of various kinds, especially those having a special affinity for chromic acid and its salts, by which they are stained brown or yellowish-brown, and hence termed **chromaffine** or **chromaphil.**

DEVELOPMENTAL ABNORMALITIES.—The most important of these is the occurrence of **Accessory Suprarenals,** which may consist of cortex alone, medulla alone, or a combination of both. They usually vary from the size of a pin's-head to that of a pea or a bean. They are situated most frequently in the immediate neighbourhood of the main suprarenal; but they may be found on the surface, or in the substance, of the kidney, or, more rarely, of the liver, along the abdominal aorta, and even in the broad ligament,[2] in the walls of hernial sacs

[1] Schäfer, *loc. cit.*, p. 54.

[2] In the ovary, the corpora lutea, or lutein-bodies, of menstruation and pregnancy have, on account of their yellow-ochre colour, not infrequently been mistaken for suprarenal "rests" and tumours. They are, of course, a normal phenomenon in the ovary, following the discharge of the ovum from its ovisac, though tumours occasionally arise from them.

(MacLennan), or in connection with the epididymis; and, in these various positions, they may give rise to tumour-formation (*see* pp. 853, 865: and also pp. 271, 273). Such aberrant suprarenals consist, as a rule, mostly of cortex, and may be recognised by their characteristic
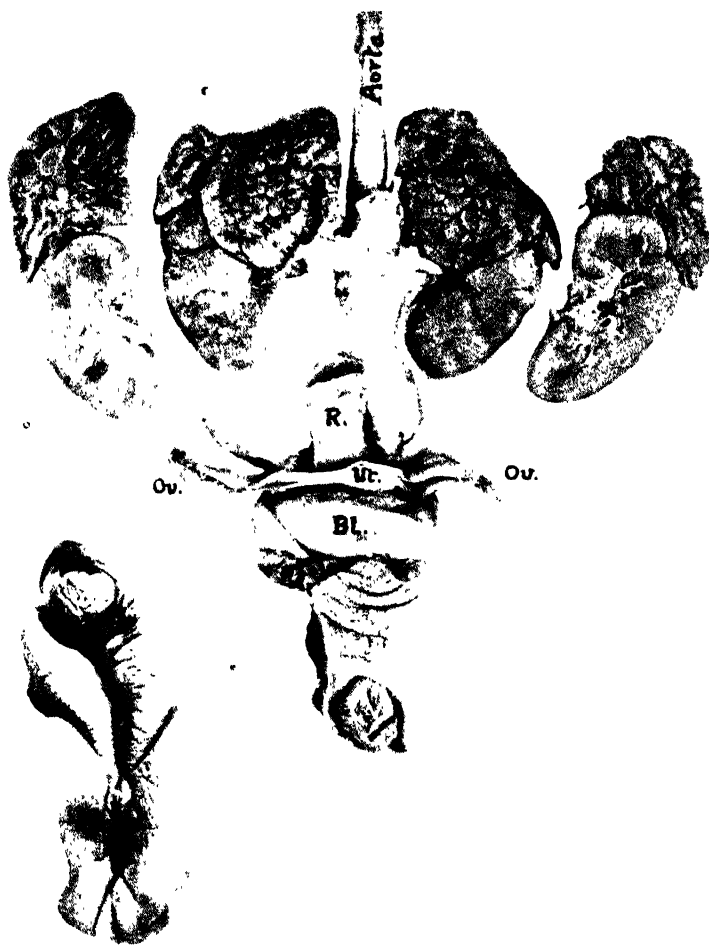
Fig. 383.— Greatly Enlarged Suprarenals from a pseudo-hermaphrodite infant, believed by its parents to be a male. The clitoris is enlarged and simulates a penis with its prepuce. (*Ut.* Fundus of Uterus. *Ov.* Ovaries. *Bl.* Bladder. *R.* Rectum.)
    Each kidney and suprarenal is cut coronally and both halves are shewn. The lower left-hand figure shews the perineum, from anus to clitoris.

ochre-yellow colour. A varying amount of medulla may occur in the larger " rests "; whilst accessory glands consisting of medulla-like structure alone are known as **chromaffine bodies** or **paraganglia.** It is interesting to note that the **Carotid Body** or **Carotid Gland** is of similar nature.

    Absence of the fœtal boundary zone has been noted in the anencephalous fœtus (Elliott and Armour), and it has been suggested that this layer

may have some influence on the development of the cerebral hemispheres, and upon the formation of the myelin of medullated nerve-fibres.

Persistence of the boundary zone and **hypertrophy of the cortex** may be associated with sexual precocity and other abnormalities, especially pseudo-hermaphroditism (*see* fig. 383), whilst castration is said to lead to cortical hypertrophy.

Malposition of the entire suprarenal gland may occur in some cases, and the organ may be partially, or even entirely, embedded in the adjoining kidney. The right suprarenal may similarly be found on the surface, or in the substance, of the liver. In cases of displacement and malposition of the kidney, the suprarenals usually do not accompany the kidneys, but are found in their normal position.

ATROPHY.—Minor degrees of atrophy are common in various conditions characterised by wasting of the body-tissues generally. For the pathological lesions and the important syndrome of symptoms found in **Addison's Disease,** *see* p. 852. Slighter grades of **suprarenal inadequacy** are not uncommon, but are of clinical, rather than of pathological, interest.

FATTY DEGENERATION is often well marked. The yellow cortex normally contains a considerable proportion of fat; and, in old age and in many diseases, this is markedly increased in amount, constituting a condition of fatty degeneration.

WAXY, or AMYLOID, DEGENERATION is often well seen in these glands. It occurs from the usual causes, and shews the ordinary method of distribution of the disease, *i. e.* in the connective tissue of the small arteries, etc.

PIGMENTARY CHANGES are common, especially in old persons, the colour of both cortex and medulla becoming much darker, apparently from increase in their normal pigment.

ACUTE CHANGES.—Cloudy Swelling is often well marked in the acute infective fevers and septicæmias. **Focal Necrosis** may occur. **Abscesses** are comparatively rare in the suprarenals, but, when found, may attain to a considerable size.

Acute hyperæmia of the glands—especially of their medullary portions, which may become much softened—occurs in acute infective diseases; and **hæmorrhages** are not uncommon, especially in some of the acute infective conditions such as scarlet fever, diphtheria, and cerebro-spinal fever, and in blood- and other diseases. Such hæmorrhage may be severe, causing destruction, especially of the medulla, and producing a hæmorrhagic distension of the gland, resembling a cyst. These hæmorrhages are sometimes bilateral, and have been described as occurring in newly-born infants.

SYPHILITIC CHANGES, though rare, do sometimes occur, especially in congenital syphilis, in which gummatous masses are occasionally found in the suprarenals.

TUBERCULOSIS of the suprarenals, in some of its forms, is very

important. The lesions in these organs may be part of a more wide-spread tuberculosis, or the suprarenals may be affected alone. Small miliary tubercles may be found in general tuberculosis, especially in children, and are of themselves of no special importance. In the adult, lesions varying in size from such small acute miliary, up to larger caseous, areas may be found, and, as long as these are scattered, they lead to no immediately serious results; but, when the condition becomes more advanced, as, for example, in **chronic caseous tuberculosis of the greater part of, or the entire, gland on both sides,** it tends to produce **Addison's disease,** owing to destruction of the glandular tissue and consequent loss of the function of the gland.

ADDISON'S DISEASE is, in the majority of cases, associated with the destruction of both suprarenal bodies, with loss of their special internal secretion. Such destruction is usually caused, as above mentioned, by **chronic caseous tuberculosis,** or, more rarely, by **chronic fibrous atrophy** of the organs. An analogous acute condition, leading to a fatal issue, may be produced experimentally in animals by the complete removal of the glands. Cases in which both suprarenals have been removed, or destroyed by disease, without the production of Addisonian symptoms may possibly be accounted for by the presence of accessory suprarenals elsewhere, or by the functioning of chromaffine tissue elsewhere, *e. g.* in the Carotid Gland. Minor degrees of suprarenal insufficiency may also occur without the full syndrome of symptoms.

The disease is commoner in males—usually during the third and fourth decades of life—and is characterised by **progressive asthenia,** with **great general muscular** and **cardio-vascular weakness** with lowered blood-pressure : **extreme emaciation : gastro-intestinal disturbances,** such as nausea, vomiting, and diarrhœa : and by certain important **pigmentary changes in the skin, mucous membranes,** and elsewhere. There is usually distinct, and sometimes severe, **anæmia,** though, in some of the recorded cases, there has been no marked diminution in the number of the red cells. The temperature is, as a rule, subnormal.

The **colour of the skin** varies from a light brownish-yellow to a deep brownish-black colour. This " **bronzing** " is due to an increase of pigment in the deeper part of the rete Malpighii and in the superficial parts of the connective tissue of the corium, especially around some of the blood-vessels. It is usually diffuse, but occasionally finely punctate, the pig-ment being, for the most part, contained **in the cells,** but also lying to some extent free in the lymph-spaces. This pigmentation is usually most marked on parts of the skin exposed to any **irritation** (*e. g.* the pressure of a belt), and to the action of light, *e. g.* the neck, face, hands, etc. An abnormal increase is also found especially in positions where cutaneous pigment **normally** abounds, viz. in the axillæ, areolæ of the nipples, external genitals, etc. Certain of the **mucous membranes** commonly shew a patchy brownish pigmentation, especially on the tongue, the inner surface of the lips and cheeks, the gums, and other portions

of the buccal mucous membrane. Patches of pigment may be found also in the conjunctivæ, vagina, and, it is said, in certain of the serous membranes. In some of the more acute cases, the bronzing of the skin may not occur.

The **heart-muscle** is usually soft and flabby, and may show marked brown atrophy. The **spleen** is sometimes enlarged and congested.

Changes in the suprarenals :—

(a) **Chronic Tuberculosis with Caseation** is the commonest lesion. **Both** organs are affected, though often in varying degree. There is extensive destruction of the glandular tissue, the organs being usually somewhat enlarged and irregular in shape. The caseous nodules are often surrounded by dense fibrous tissue due to chronic proliferative inflammatory changes, which tends to produce adhesions to the surrounding fat, etc. **On section,** they may be firm and fibrous, or softer and more caseous. Fibroid bands may be found among the caseated débris, and the latter may undergo calcification.

The disease is not necessarily associated with any tuberculous disease elsewhere, though this is not infrequently found in other parts of the body, for example in the lungs, joints, spine, glands, etc.; yet, in ordinary cases of tuberculosis, there may be wide-spread tubercles throughout the body and perhaps none in the suprarenals. It is, therefore, difficult to explain why these two organs should, in certain cases, be specially attacked by tuberculosis, as they are far apart and small in size. It is possible, indeed, that they are rendered liable to such attack by the presence of some other previous, as yet unrecognised, primary lesion.

(b) **Chronic Fibrous Atrophy** may also, but much more rarely, produce the condition of Addison's disease. This change is a chronic fibrosis with extreme atrophy of the glandular structure, analogous to the changes observed in the thyroid gland in myxœdema. In such cases, it is sometimes difficult to discover the fibrous remains of the atrophied suprarenals, unless the arteries be traced to them.

(c) A clinical picture, similar to, and even indistinguishable from, that of Addison's disease, has occasionally been found in certain cases in which the suprarenals have appeared to be unaffected. In some of these, the **semilunar ganglia** and other parts of the solar plexus have been the seat of degenerative conditions, especially fibrosis. This has led to the view that Addison's disease may be produced by lesions other than those affecting the suprarenal bodies; but it is possible that, in cases implicating the solar plexus and neighbouring parts, the vascular or lymphatic supply of the suprarenals may have been interfered with by the contraction of fibrous tissue in the neighbouring structures, and their secretion prevented from passing into the circulation.

TUMOURS OF THE SUPRARENALS.—Both suprarenals are sometimes the seat of **tumours,** e. g. adenomata, or, occasionally, sarcomata. These, however, do not produce the classical symptoms of Addison's disease, perhaps because sufficient suprarenal tissue is left in an actively

secreting condition: or because the tumour-tissue derived from the suprarenals may contain or produce—imperfectly and aberrantly, it may be—sufficient internal secretion to prevent the occurrence of the disease. The commonest neoplasm of the suprarenal is a variety of **adenoma**—usually arising from an aberrant portion of the gland embedded in the kidney or, more rarely, in the liver. These tumours, arising from the **suprarenals** and **suprarenal** "**rests,**" in which the original structure of the organ is more or less recognisable, have been termed **hypernephro-mata.** Their occurrence in connection with the kidney is described on

FIG. 384.—*Mixed Malignant Tumour of Kidney*, probably originating from the inclusion or intermingling of neighbouring tissues during embryonic life. The tumour contains areas of imperfectly-formed cartilage, small cystic adenomatous spaces, and masses of aberrant suprarenal tissue. The dark areas are due to extensive hæmorrhages into the tumour. (Edinburgh University Anatomical Museum. Catalogue No., Gen.-U. A. w. viii. 3.)

p. 917. They may be **simple** or **malignant,** and, in the latter case, are frequently mixed with cartilage and other tissue-elements, forming one variety of the so-called **mixed congenital tumours** (*see* fig. 384).

To Professor E. E. Glynn, who has done much valuable work on the subject, we are indebted for the following note upon **Tumours of the Suprarenal :**—" Primary or secondary neoplasms are rare. The three commonest **primary tumours** are :—(*a*) **Single** or

multiple cortical adenoma. Occasionally, **diffuse bilateral hyperplasia** of both cortices occurs—sometimes in pseudo-hermaphroditism (*see* fig. 383).
(*b*) **Gliosarcoma** or **neurocytoma,** derived from the medulla: it is invariably malignant, and, in children, frequently produces cranial metastases, sometimes with exophthalmos (Hutchinson's type): or, if it occurs congenitally, infiltrations in the liver (Pepper's type). These growths, when stained by the usual methods,*resemble a small round-celled sarcoma. (*c*) **Suprarenal Hypernephroma** or 'Carcinoma' (many authors call them 'sarcomas')—these tumours may produce change in secondary sex-characters, or **Suprarenal 'Virilism.'** In children, there is probably invariably precocious growth, usually obesity, hirsutes, *i. e.* premature growth of pubic hair and often abnormal development of
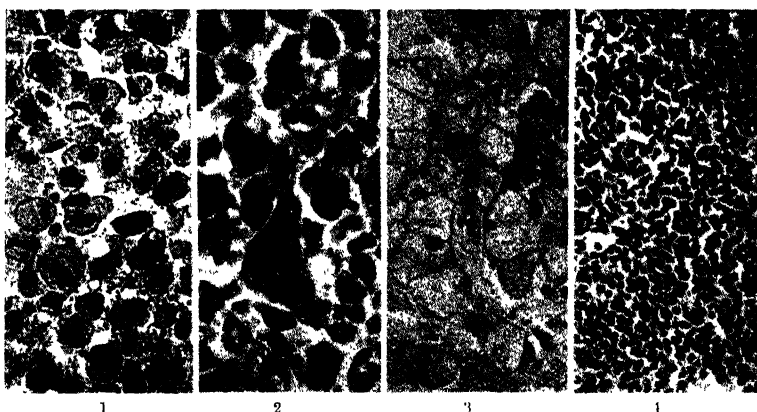
FIG. 385.—Microscopical Appearance of certain suprarenal tumours (stained with hæmatoxylin and eosin).

(Lent by Professor Ernest Glynn, Liverpool.)

1. Suprarenal Cortical Tumour, simple or typical. × 300.
2. Suprarenal Cortical Tumour, malignant or atypical. × 200.
3. " Renal Hypernephroma." × 300.
4. Suprarenal Medullary Tumour or Neurocytoma, *i.e.* composed of nerve-tissue. × 300.

hair on the face and body, also hypertrophy of the external genitals, but rarely sexual precocity; in women, before the menopause, facial hirsutes is common, menstruation may cease, the uterus, ovaries and breasts may atrophy, and, occasionally, the voice cracks.

"The tendency of **cortical enlargement** to increase 'maleness' is emphasised by their much greater frequency in female than in male pseudo-hermaphrodites.

"Chiefly owing to the development of the cortex from mesothelium, these tumours may resemble either cancer or sarcoma—occasionally both in the same section; some indefinitely recall the structure of the suprarenal cortex; but all are unlike the ordinary 'renal hyper-nephroma.' Adami classifies them as mesotheliomas. The majority are malignant."

DISEASES OF THE PITUITARY BODY

(Hypophysis Cerebri)

The **hypophysis cerebri** is a small, somewhat flattened, greyish-red body, which lies in the pituitary fossa or sella turcica of the sphenoid bone at the base of the skull. It consists of a larger, **anterior** or **glandular,** stomatodæal portion; in intimate relation with which lies the smaller, **posterior part,** which is connected with the floor of the third ventricle by a delicate, soft, easily-ruptured stalk of nervous tissue—the **infundibulum.** Both of these portions arise originally as hollow diverticular processes, the lumina of which, in course of time, in the human subject, usually become obliterated; though parts of them—especially that of the glandular portion sometimes persist, and may occasionally become distended and form **cysts,** the lining cells of which may shew cilia. In its phylogenesis, the gland is originally an organ which is situated at the anterior end of the central nervous canal, into which it poured its secretion.

On microscopical examination, the area anterior to the original cleft or diverticular hollow of the **glandular portion, or pars glandularis,** consists of alveolar spaces loosely filled with glandular epithelial cells. Some of these cells are clear and non-granular (chromaphobe), but the larger number are granular and stain well (chromaphil). The majority of the granular cells exhibit a marked oxyphil or eosinophil reaction to acid dyes such as eosin, whilst in others the granules are more basophil. Fine fatty globules are also present in most of the cells. Between the alveoli, there is a very rich plexus of blood-capillaries or sinus-like spaces, and also lymph-spaces, the lymphatic vessels from which join those in the fibrous tissue of the capsule. The narrow layer of glandular tissue lying between the original cleft and the posterior lobe of the organ forms an intermediate or boundary layer, or **pars intermedia,** in which the cells are often arranged in more distinct acini, in the form of closed vesicles, some of which may become distended with a colloid substance, giving the spaces a morphological resemblance to those of the thyroid gland. The cells of the pars intermedia may intermingle to some extent with the adjacent neuroglia-fibres of the pars nervosa, as far as the continuation of the third ventricle into the infundibular stalk; and do not possess coarse eosinophil granules.

The **posterior portion,** sometimes, because of its embryological origin, termed the " nervous " lobe, or **pars nervosa,** consists of a loose stroma, chiefly composed of neuroglia-fibres, in which are embedded numerous spindle-shaped and irregular, branching cells, many of which contain granules of pigment. Herring regards these cells as neuroglial, and denies the occurrence of nerve-cells described by some writers.

CONGENITAL ABNORMALITIES.—In addition to various cysts which may arise from the persistence within the organ itself of the primitive intra-glandular cleft, traces of the original connection with the buccal ectoderm may be occasionally found, e. g. under the mucous membrane of the pharynx as the so-called **pharyngeal hypophysis :** within the bone of the basi-sphenoid : or in the dura lining the sella. These, in rare instances, give rise to tumours or cysts.

INTERNAL SECRETIONS PRODUCED BY THE PITUITARY.—Though they probably exist, and have an important bearing on the development of the bones and other tissues of growing animals, no definite autocoids have as yet been demonstrated in the anterior portion; but from the

posterior lobe, including the pars intermedia, the active principles have been extracted, and are sold commercially as **pituitrin** or **hypophysin.** These contain probably more than one autacoid, though some authorities regard the results produced as due to the varied action of one substance. Its injection produces a marked rise of blood-pressure, with contraction of vessels, including those of the heart and lungs, due to direct stimulation of their muscle : increase in the force of the individual heart-beats, even if the vagi are cut or paralysed : contraction of the plain muscular tissue of the stomach, intestine, bladder and uterus : dilatation of the renal vessels, and increased secretion of urine due to direct stimulation of the kidney-cells : increased secretion of cerebro-spinal fluid (Herring is of opinion that the secretion of the pars intermedia finds its way into the cerebro-spinal fluid) : and increased flow of milk, from contraction of the alveolar walls and ducts, without special increase in its daily amount : and dilatation of the pupil. Glycogen disappears from the liver. Medicinally, pituitary extract is valuable in the treatment of surgical shock, post-anæsthetic collapse, and intestinal and uterine inertia, etc., its action being a direct one upon the involuntary muscle-fibres themselves. After removal of the thyroid, the pituitary becomes enlarged and altered, the colloid-containing vesicles usually developing, and the pars intermedia shewing increased activity in the production of the hyaline and granular masses which pass from it through the pars nervosa into the infundibular extension of the third ventricle. There are also intimate connections between the functions of the pituitary and those of the suprarenals, pancreas, liver, and sex-organs. During pregnancy and menstruation, the pituitary undergoes marked enlargement. The feeding of poultry on anterior pituitary substance has been found to increase greatly their egg-laying capacity.

Experimental extirpation of the gland in animals has proved that the organ is essential to life. Complete removal of the anterior lobe is speedily fatal; but extirpation of the posterior nervous part alone does not appear to cause any very profound disturbance, even after several months. When the whole gland has been removed, death occurs in a few days, the animal becoming lethargic and refusing food, losing muscular tone, respirations and pulse becoming slow and feeble, temperature subnormal, and coma supervening. In cases of incomplete removal in young animals, development is markedly retarded, the animals remaining small, dull and apathetic, the sexual organs infantile, and ossification imperfect, but with a marked tendency to the occurrence of adiposity, and increased toleration of sugar—the secretion of the posterior lobe being " essential to effective carbohydrate metabolism " (Cushing)– with glycosuria and polyuria, the latter often persisting after the former has passed off.

The anterior lobe of the pituitary gland is subject to **toxic** and other **degenerative changes** similar to those found in other glandular organs. Thus, cloudy swelling, focal necrosis, acute and chronic congestion, hæmorrhage, waxy degeneration, etc., may be found in it. The most important lesions in this organ, however, are those associated with the disease known as **Acromegaly,** and also with the closely-allied condition of **Gigantism.** Since these two conditions were discovered to be due to the excessive function of the pituitary body, a number of other obscure conditions have come also to be attributed to abnormalities of the organ. Harvey Cushing [1] classifies these under the following headings : **Dyspituitarism,** any disorder of the gland ; this usually begins with enlargement

[1] Cushing, *The Pituitary Body and its Disorders,* 1910.

of the anterior lobe, accompanied by symptoms due to excessive function or **Hyperpituitarism** (*see* below); followed eventually, after a varying period, often prolonged, by gradual diminution—**Hypopituitarism** —or even complete loss—**Apituitarism**—of the functions of the gland. These will be best understood from a description of the condition known as **Acromegaly,** in which the disease supervenes *after* the ossification of the epiphyseal cartilages, whereas, in Gigantism on the other hand, these are unossified and the bones can still grow in length.

Fig. 386.—*Acromegaly.* Typical case shewing the characters described in the text. Note especially the enlargement of hands and feet, the large coarse features of of the face, etc.

ACROMEGALY was first recognised as a separate disease in 1886 by Pierre Marie, who distinguished it from such conditions as myxœdema, osteitis deformans, and leontiasis ossea. It is specially characterised by **enlargement of the extremities**— hands, feet, and certain parts of the head (*see* fig. 386)—(hence the name, from ἄκρον, a point or extremity : μέγας, large), the increase being not only in the bones, but also in the overlying soft parts. The increase of the **hands** and **feet** is in breadth and thickness rather than in length, the fingers being clumsy and sausage-shaped, and the great toe usually more markedly enlarged in proportion to the other toes.

The forearms and legs are, as a rule, not specially increased. The **bones of the skull,** and especially those of the **face,** particularly the **jaws,** are enlarged, the lower jaw being usually most affected, and often elongated and projecting much beyond the upper, so that the teeth cannot be approximated. The bony prominences and ridges are exaggerated, and the skull comes to resemble somewhat that of a gorilla. The **ears** and **eyelids,** the **nasal bones** and **cartilages,** and the **lips** and **tongue,** are increased in size and thickness; and these various changes, together with the **thick, coarse character of the skin,** produce a very typical picture. The skin often shews numerous **warty excrescences** and **pigmented moles,** and the **hair** is long and coarse. The **spinal column** frequently shews **kyphosis** or other type of curvature; and the **ribs, sternum,** and **pelvis** are usually enlarged and thickened. The **abdomen** is often protuberant, and many of the **internal organs,** *e. g.* the stomach, may shew great enlargement—the so-called **splanchnomegaly.** In the female, the uterus is usually atrophied.

During life, such cases, as a rule, present great **muscular weakness** (though there may be a preliminary period of hypertrophy and increased strength), **polyuria** in thirty to fifty per cent. of the cases, combined with **glycosuria** (these two symptoms being due probably to involvement of the pars intermedia), sometimes **albuminuria,** and excessive **perspiration.** **Bi-temporal hemianopsia** and **headache** may be associated with the **pituitary enlargement** which is practically always present, usually affecting chiefly, and in some cases only, the anterior lobe. This may be the seat of a simple **hyperplastic enlargement,** with little apparent alteration in structure, or, in other cases, **carcinoma** or **sarcoma** may be present. **Cystic changes, fibrous atrophy,** and **gummatous** and **tuberculous disease,** have each also been described in certain of the cases, but appear to be less common causes of the disease. The **sella turcica** is, as a rule, very considerably enlarged—a fact usually ascertainable on X-ray examination—and, in the case of malignant tumour of the gland, the bones and the base of the brain may become infiltrated by the growth. Implication of the **optic tracts** or **commissure** may lead to the occurrence of bi-temporal hemianopsia already mentioned, or even to complete optic atrophy. If secondary degenerative changes or hypoplasia of the gland occurs, the symptoms of hypopituitarism may supervene (*see* below). Every case of tumour of the gland need not necessarily develop acromegaly or gigantism, as partial or complete destruction of the organ may occur in place of increase of its functions.

In a proportion of cases of acromegaly, there are also lesions present in certain other glands. The **thyroid** may be enlarged, or in some instances atrophied, and **mixed cases of acromegaly and myxœdema** have been described. The **thymus** has been found persistent and enlarged in a few cases, and changes may also be present in the **salivary glands, pancreas,** etc.

The **blood,** in three cases of this disease examined by one of the

authors, shewed a distinct and persistent increase in the number of red cells, with a moderate diminution in the amount of hæmoglobin, and a comparatively low leucocyte-count. On differential examination, the latter shewed great diminution of the small lymphocytes, and a remarkable increase in the number of large mononuclear cells. A slight increase in the number of mast-cells was also present from time to time, and occasionally exceeded one per cent. in individual counts.

GIGANTISM.—When changes analogous to those found in acromegaly occur in the pituitary **early in life,** before the ossification of the epiphyseal cartilages is complete, the bones may undergo **elongation** as well as increase in thickness, the condition of **Giantism** or **Gigantism** resulting. Such "giants" are usually delicate and weakly, though occasionally their muscular development is in proportion to their increased stature. They usually die comparatively young; or, if they live, they may later develop the typical symptoms of acromegaly.

HYPOPITUITARISM.— Pituitary insufficiency may be due to disease or accident (c. g. the case of a bullet lodging in the sella turcica), and reference has already been made to experimental removal of the gland. Hypopituitarism is characterised by the clinical picture described by Fröhlich in 1901, to which Bartels gave the name **dystrophia adiposogenitalis,** and in many ways resembling the results of incomplete removal in young animals. If pituitary insufficiency supervenes **before adolescence,** the stature remains small, and is associated with infantilism and adiposity, and the male may shew "**feminism,**" e. g. broad pelvis, small hands and feet, tapering fingers, some degree of *genu valgum,* absence of beard, hair limited to the mons veneris, and sometimes marked development of the breasts. In the female, the menses are irregular or absent. The epiphyseal cartilages persist. The skin is smooth and thin and deficient in secretion, and the nails are small, thin, and with their lunules absent. There is unusual tolerance of sugar, which assists in the production of the adiposity. Arterial blood-pressure is low, the heart-beat slowed, and there are often drowsiness, torpidity, and mental derangements. If the disease supervenes **after adolescence,** the chief phenomena are lowered temperature, abnormally increased tolerance of sugar, adiposity, and, in the male, the replacement of the normal trichosis by that of feminine type. A pigmentation of the skin somewhat resembling that of Addison's disease may occur. Just as myxœdema may supervene in cases of exophthalmic goître when atrophic changes occur in the previously hyperplastic thyroid, so may patients suffering from hyperpituitarism come later to shew symptoms of pituitary insufficiency if atrophy of the pituitary supervenes on the previous hyperplasia. The adiposity of hypopituitarism is due probably to deficiency of the posterior lobe; whilst dwarfism, on the other hand, is, in many cases, due, in all likelihood, to insufficiency of the anterior portion of the gland.

The **PINEAL BODY (Epiphysis cerebri)** is a small, reddish structure, about the size of a cherry-stone, situated in relation to the posterior part of the third ventricle, from which it projects downwards and backwards between the superior pair of corpora quadrigemina. It is developed from an evagination of the wall of the third ventricle, from which evagination, in certain reptiles, a median or third eye originates. The pineal is relatively larger in the child than in the adult, and in the female than in the male. Its structure varies considerably in different cases, but it usually shews a number of saccular, or, in some cases, somewhat tubular spaces, more or less filled with epithelial cells, and with large capillary or sinus-like blood-channels between the spaces. Most of the cells shew fine oxyphil granules, but some shew basophil granules. The stroma consists of neuroglia, and the whole is invested with a pial covering. The organ undergoes considerable retrogression after puberty. The follicles also very frequently contain aggregations of calcareous particles (the so-called '' **brain-sand** ''), which may sometimes be present in marked excess.

Injection of pineal extract produces a marked, but temporary, fall in blood-pressure (Schäfer), otherwise the results have been mainly of negative character. Foa, however, states that cockerels grow more rapidly under its administration and shew earlier development of the testicles and secondary sexual characters. Similar sexual precocity and increased stature have been noted in boys suffering from some forms of pineal tumour— sometimes associated with extraordinary precocious mental development. •

The only pathological lesions of importance originating from this structure are certain **tumours**. These may be of the nature of simple enlargements, usually with excess of the gritty particles above referred to (psammomata). **Cystic growths** also occasionally occur; and **teratomatous** and **mixed tumours** containing cartilage and gland-like elements, sometimes combined with sarcomatous structure, have been described.

The **CAROTID** and **COCCYGEAL GLANDS** are rudimentary glandular structures, the functions and significance of which are unknown. The former are probably paraganglia, related in development to the series of chromaffine bodies of which the suprarenal medulla (*q. v.*) is an example. The coccygeal gland does not belong to this series, and probably represents an arterio-venous anastomosis seen in some of the lower mammals. These structures may occasionally give rise to **tumour-growth.**

DISEASES OF THE GENITO-URINARY SYSTEM

A DETAILED description of the normal anatomy and histology of the different parts of the genito-urinary system would be out of place in a text-book of Pathology. It will be convenient, however, when we come to describe some of the structural alterations in the kidneys, to give a brief outline of the minute anatomy of these glands (p. 869).[1]

DISEASES OF THE KIDNEY AND ITS PELVIS

The ureter, the pelvis of the kidney, and the renal tubules, arise developmentally as a tubular diverticulum or outgrowth from the lower end of the duct of the Wolffian body or mesonephros—the primitive excretory organ of the embryo before the development of the permanent kidney.

CONGENITAL ABNORMALITIES OF THE KIDNEY :—

1. CONGENITAL MALFORMATIONS.—The most important of these conditions is **coalescence** or **fusion of, or a junction between, the two kidneys.** Each of the affected organs may be situated in its normal position, but, in the majority of cases, one or both may be displaced downwards. In the most usual form of this malformation—the **horseshoe-kidney**—the lower, or, much more rarely, the upper, ends of the two organs are united across the vertebral column (see fig. 387). The uniting band is, in some cases, composed of true kidney substance, sometimes of considerable thickness; whilst, in other instances, it consists of fibrous tissue in which there is no trace of glandular structure. As already stated, the union is most frequently between the lower ends of the two kidneys. Each half of the fused mass is usually provided with a single **ureter,** which passes down **in front** of the uniting bridge. Sometimes, however, one or both of the ureters may be double, occasionally throughout the entire length, but, more usually, only towards the upper end. There are, as a rule, two distinct pelves, which are, in almost all cases, situated towards the **anterior** aspect of the combined organ (see fig. 387).

A less common variety of fusion is that known as **Sigmoid Kidney,** where the two organs form a continuous or sigmoid curve, one kidney

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[1] For a detailed account of the more surgical conditions of this system, the reader is referred to such textbooks as J. W. Thomson Walker's *Genito-Urinary Surgery* (Cassell & Co., Ltd., London, etc., 1914), especially for the appearances on Cystoscopic Examination, Radiography, etc.

being situated below the other, and the line of fusion running vertically between the two corresponding ends. This variety may be regarded as a horseshoe-kidney which has been partially rotated so that the concavity is turned to right or left instead of upwards.

Sometimes the fused organs are considerably displaced, the mass lying, it may be, towards one side of the abdomen, or even at the brim, or in the cavity, of the pelvis.

2. **ABNORMALITY IN NUMBER.**— The presence of a **third kidney**
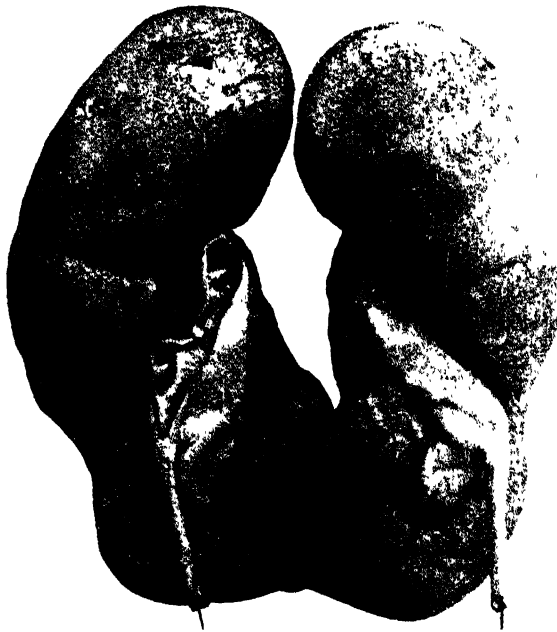
Fig. 387.—*Horseshoe-Kidney.* The lower ends of the organs are united by a thick bridge of glandular tissue passing across the middle line. The ureters (into which bristles have been inserted) pass down anteriorly. (Edinburgh University Anatomical Museum. Catalogue No., Gen. U. A. a. 1.)

is an extremely rare condition. Occasionally, only one kidney is found —the so-called **Solitary Kidney.** When the other organ is *entirely* absent, the ureter and the renal vessels are also absent on the same side. In some cases, traces of the other kidney are present, and may be discovered by following the course of the vessels or ureter, which, in such cases, may not be entirely absent.

The **Solitary Kidney** may be increased in size, but this is by no means essential. Its vascular supply is often abnormal, for example it may receive branches from the iliac or other arteries. In health, this single kidney may effectively carry on the work of renal secretion; but, if it

becomes the seat of tuberculous disease, or if impaction of a calculus occurs in its pelvis or ureter, or if, from any other cause, its function is interfered with, the results will naturally be more serious than if there were another kidney to aid in the process of excretion.

3. **INEQUALITY IN THE SIZE OF THE TWO KIDNEYS** may be a **congenital** condition arising from arrested development or from disease during intra-uterine life; or it may occur **later in life** from disease, for example, from the **impaction of a calculus** producing loss of function and atrophy on one side. Similarly, **localised vascular lesions** may interfere with the normal growth of the kidney in young subjects, or with the maintenance of its nutrition in the adult. Other causes of inequality in the size of the two organs will be described under such headings as **Tumours, Cysts, Inflammation,** etc.

4. **ABNORMALITIES IN THE SHAPE OF THE KIDNEYS, and IN THE ORIGIN OR DISTRIBUTION OF THEIR BLOOD-VESSELS,** are frequently found in conjunction with the foregoing conditions. The **genital organs** may or may not shew associated abnormalities, for example they may be rudimentary, or even absent, on the same side as the affected kidney.

5. **ABNORMALITY IN POSITION.**—This may be **congenital** or **acquired.** In **CONGENITAL MALPOSITION —dystopic kidney** —all degrees of displacement may be found, from cases in which it is comparatively slight to those in which the organ may be found just above, at, or even below, the brim of the pelvis. It may lie over the sacro-iliac joint, or in the hollow of the sacrum **(Sacral Kidney).** In the female, such abnormalities in position may lead to interference with parturition, and render the displaced organ very liable to injury during the process. The **corresponding suprarenal body** is usually not associated with the kidney in such displacements, but is found in its normal position, and possesses its normal vascular supply; whereas the origin of the vessels supplying the dystopic kidney is displaced downwards, e. g. they may arise from the lower part of the aorta, the common or internal iliac, the middle sacral, or the inferior mesenteric artery. The kidney-tissue may be normal or diseased, and there may be associated defects in the bladder, rectum and genital organs, which, if unilateral, occur on the same side as the affected kidney.

MOVABLE or FLOATING KIDNEY—NEPHROPTOSIS.—All degrees of this condition may be found, from a slight increase in the normal mobility up to cases in which the organ—most commonly the right—can be moved to almost any part of the abdominal cavity. This mobility is due usually to an abnormal laxity of the peritoneal and fascial investments covering the anterior surface, and of the fat and cellular tissue around the organ. The kidney may have an incomplete peritoneal covering, or may, in rare cases, even possess a complete investment and mesentery containing the renal vessels and ureter. In some cases, the condition

appears to be a **congenital** one ; but in others, it is an **acquired** abnormality, the most frequent cause being **repeated pregnancy,** especially when combined with great relaxation of the abdominal parietes, etc., or where there has been **absorption of the perinephric fat** which helps to support the kidney in position. The condition is, therefore, found most commonly in women. The **right** kidney, as already stated, is more frequently affected than the left; and it is very rarely that both organs are freely movable. Occasionally, the displaced kidney may become adherent in some abnormal position ; or again, torsion of the vessels and of the ureter may occur.

6. **PERSISTENCE OF FŒTAL LOBULATION** is of extremely common occurrence, but is of little pathological importance. It is due to incomplete fusion of the lobar divisions in the fœtal kidney, which divisions should normally disappear. All degrees of this condition may be found, and, when slight, should not be mistaken for the depressions caused by the absorption of old infarcts, retention-cysts, etc. The capsule is adherent to the septa between the persisting lobes; and such organs frequently shew one or more medium-sized arteries penetrating the kidney substance between these lobes.

7. **ABNORMALITIES OF THE URETERS** occasionally occur, for example, **doubling**—which may be partial or total—**abnormal origin,** etc. The ureters may be involved in congenital abnormalities of the bladder; and, occasionally, they may even open into the rectum. **Twisting** or **abnormal bends** on the ureter may lead to hydronephrosis (*see* fig. 388).

Congenital dilatation of one or, more usually, both, ureters, sometimes extreme in degree, is occasionally found, often without any obvious cause and where no obstruction to the outflow of urine from the ureter itself, or from the bladder, can be demonstrated.

8. " **INCLUSION** " **OF SUPRARENALS.**—This may vary from **partial adhesion** or **fusion** of the suprarenal body up to its **total inclusion within the glandular substance of the kidney.** Abnormal portions or **supernumerary suprarenals** not infrequently occur as inclusions within the kidney, the main suprarenal body being found in its usual position. These suprarenal inclusions or " rests " may, later, become the site of tumour-formation.

9. **CYSTIC DISEASE OF THE KIDNEY.**—(Synonyms: **Cystic** or **Polycystic Kidney, Cystic Degeneration of the Kidney.**)—Two varieties of cysts in the kidney may be met with, viz. (1) those which are **primary,** and apparently congenital; and (2) cysts which are **secondary** to other diseased conditions. It is to the former of these that the term **Cystic Kidney** is specially applied. This condition may be found well advanced in the fœtus *in utero*, and may, owing to the large size of the affected organs, sometimes cause obstruction to parturition, and necessitate the evisceration of the fœtus. The disease is not confined to any special age, but may be found even in very old persons. If uncomplicated

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by other renal disease, it may give rise to no definite symptoms during life, and kidneys shewing advanced cystic disease may be

FIG. 388.—Hydronephrosis arising from twisting and abnormal kinking of the ureter.

found on *post-mortem* examination in cases where its presence had been quite unsuspected during life. It is difficult to affirm positively that, in every instance, the condition has been a congenital one, and has not developed later, *i. e.* during extra-uterine life. The

disease is slowly **progressive, and, in all cases, affects both organs,** though sometimes not to a similar degree. The kidneys may be greatly enlarged, *e.g.* they may measure some six to eight or nine inches in length, the general shape of the organ being usually preserved. Projecting from the surface, and studded throughout the substance of the kidney, are innumerable cystic spaces, varying in size from some which are just visible to the naked eye, up to those about as large as a pea

A.   B.
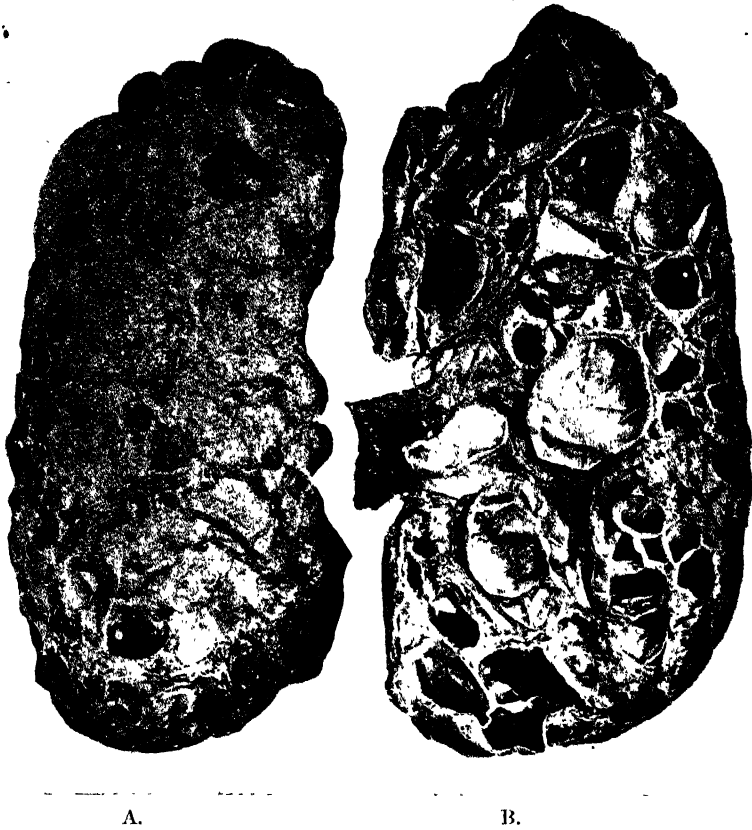
Fig. 389.—*Cystic Kidney.* A.—Outer Surface. B.—Section.

or a marble or slightly larger. They are lined by a layer of simple, flattened epithelium, and their contents—which may be fluid, mucoid, or colloid in consistence—vary in colour, and may be clear and colourless, yellowish, or brown or reddish-brown from the presence of altered blood-pigment. Most of the cysts do not contain any of the special urinary constituents, though traces of urea may be found in some of them. Although, **on naked-eye examination,** there may appear to be almost no normal secreting glandular tissue left between the cysts, yet, **microscopically,** a considerable amount may be found stretched and distended around

them. In most cases, there is sufficient kidney-substance present to enable the organs to carry on their functions more or less efficiently. In other cases, uræmia may supervene, either from the progress of the disease itself, or from some intercurrent affection of the organs.

Ætiology.—Several hypotheses have been suggested with regard to the causation of the condition. Virchow was of opinion that it was
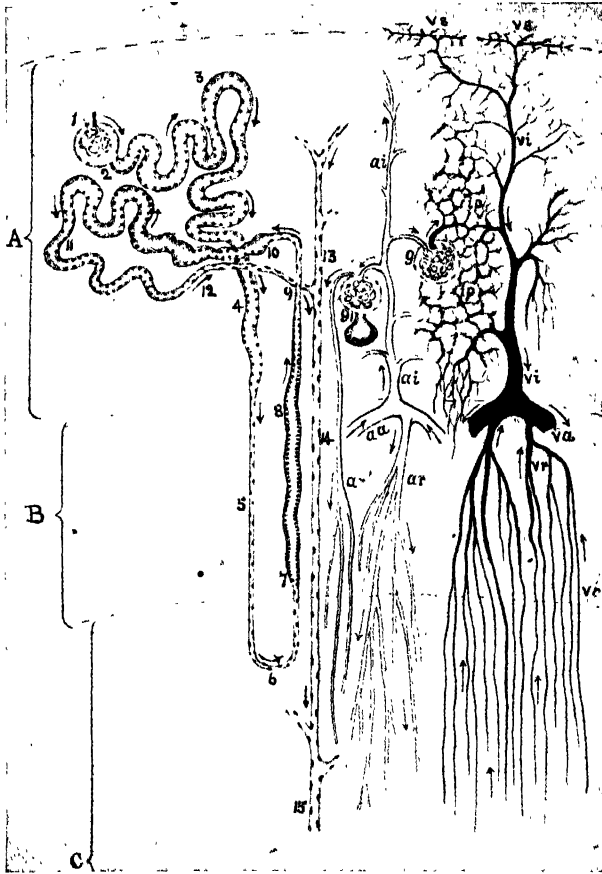
FIG. 390.—*Diagrammatic representation of the Structure and Blood-Supply of the Kidney.* A, cortex; B, boundary zone; C, medulla. (For detailed description *see* text.)

caused by inflammatory changes and interstitial overgrowth of fibrous tissue, leading to compression of the tubules and to their subsequent distension above the sites of constriction, *i. e.* a sort of chronic interstitial nephritis. This explanation appears an unlikely one, both from the clinical, and from the histological, study of such cases. Other pathologists are of opinion that it is produced by " embryonic intermingling " of the meso- and meta-nephros—the primitive and the permanent excretory organs respectively—which are developed in close proximity

to one another.   A third suggested explanation is that, early in development, some of the tubules of the kidney may not succeed in effecting a junction with the corresponding glomeruli which should grow out from the mesothelium to meet them; or that the cysts may possibly arise from excess in number either of the tubules or of the glomeruli, with subsequent distension of the supernumerary structures.

It is not very uncommon in cases of cystic kidney to find an **associated cystic condition** of the **liver,** or, more rarely, of the **pancreas,** or of some other organ.

INJURIES OF THE KIDNEY

Contusion and rupture of the kidney may result, **without external wound,** from a direct blow on the loin or over the lower ribs, or from indirect violence such as a fall upon the buttocks or forcible flexion of the body.   The capsule may or may not be involved in the tear, and the effusion of blood and urine will be subcapsular or extracapsular accordingly.   Lacerations may be of all degrees, from a slight crack to an extensive tear, and are usually transverse or slightly oblique, and most frequently on the anterior surface.   The pelvis and renal vessels may be involved, and the ureter may be ruptured, with varying results.   The commonest symptoms are **shock,** usually severe, but sometimes delayed in slighter cases, **pain, swelling,** and **hæmaturia** (in over ninety per cent.). Healing of lesser degrees of rupture usually occurs rapidly by vascularisation and organisation of the extravasated blood, and fibrous-tissue formation, the contraction of the latter resulting in a scar somewhat resembling that of an old infarct.   In some cases, blood-clot may block the ureter, leading to **traumatic hydronephrosis**, which may also result from cicatrisation of fibrous tissue.   **Bacterial infection** sometimes supervenes in such cases, either from below or *viâ* the blood-stream.   Injury to the kidney in association **with an external wound,** *e.g.* due to stabs or bullet-wounds, is almost always accompanied by **infection,** and, in addition to hæmorrhage and escape of urine, prolonged suppuration may follow.

STRUCTURAL DISEASES OF THE KIDNEY [1]

In the various **vascular, inflammatory,** and **degenerative diseases** to which the kidneys are specially liable, **both** organs are almost invariably affected—though not necessarily to the same extent or degree—as, from their anatomical relations and physiological functions, they are subject to practically identical conditions, for example, the necessity of excreting from the blood certain substances, normal or abnormal, which may have an irritating and deleterious effect upon their exceedingly complex and delicate structure.   **All** the component tissue-elements of the kidney may be, and most commonly are, simultaneously affected throughout

[1] For the classification and descriptions of these diseases, the authors are indebted largely to Greenfield's " Résumé of Renal Pathology " in the New Sydenham Society's *Atlas of Illustrations of Pathology,* 1877.

the organ, though usually **in varying degree.** Thus, in some cases, the **glomeruli** may shew relatively greater changes than the other structural elements, whilst, in other instances, either the **tubules,** the **vessels,** or, it may be, the **interstitial tissue,** may exhibit pathological changes which are relatively more marked in any one of them than in the other constituent tissues. In order properly to understand these pathological variations, it is of importance to have a clear conception of the **normal structural arrangement of the kidney-tissues,** of which the following summary may be given.

Each organ is built up of an enormous number of what may be regarded as **elongated, conical, compound glands,** closely packed side by side, each with its base at the surface of the organ, and its apex at the summit of one of the Malpighian pyramids, the whole organ being invested by a strong but thin and transparent, comparatively non-adherent, fibrous membrane or **capsule.** All these **kidney-elements** or **primitive cones** have a similar structure, each being grouped around its corresponding collecting tubule.

Each **kidney-tubule** (*see* fig. 390) commences as a spherical dilatation, known as . **Bowman's capsule** (1), into which hangs the capillary tuft or **glomerulus** – capsule and glomerulus being together known as a **Malpighian body** or **Malpighian corpuscle.** The capsule opens by a narrow **neck** or constriction (2), into the **proximal convoluted tubule** (3), which is situated in the cortex, usually in close proximity to its own glomerulus. It then, as the **spiral tubule** (4), becomes less convoluted, and enters a medullary ray in which it descends. At the junction of the cortex and the medulla it becomes much narrower, and passes straight down through the boundary zone of the pyramid as the **descending limb of Henle's loop** (5). Towards the apex of the pyramid, it turns suddenly upon itself (6), and passes up again as the **ascending portion of the loop** (7–8), which, when it re-enters the boundary zone (at 7), again becomes wider and is lined by columnar secreting epithelium. It emerges in the cortex as the **irregular tubule** (8-9), which, in turn, becomes the **distal convoluted tubule** (10, 11, 12). This then re-enters the medullary ray as the short **junctional tubule** (12), which joins one of the **collecting tubules** (13–14), several of which unite and pass down in the medullary ray. Near the apex of the pyramid, several of these larger collecting tubules join to form one of the **excretory ducts** or **tubes** (15), several of which open into one of the calyces of the ureter at the apex of each papilla.

The character of the **epithelium** lining these different parts of the uriniferous tubules **varies greatly in structure and in function,** a point of extreme importance pathologically, as it may suffer damage in very varying degree at different parts in the course of the tubule. The interior of Bowman's capsule is lined by a continuous layer of flattened **endothelial** cells, which closely resemble vascular endothelium, not only in structural appearance and development, but also in their pathological reactions. This layer of cells is situated upon a delicate basement-membrane, which, in turn, is supported externally by a fine layer of connective tissue. The proximal and distal convoluted tubules, the secreting or ascending portion of Henle's loop, and also the spiral and irregular tubules, are lined by very **highly endowed columnar secreting epithelium.** The cyto-reticulum of these cells is very distinct, and true cell-granules may be demonstrated by special staining methods. The protoplasm shews vertical striation towards the deeper part of the cell. These cells interlock irregularly, but are probably distinct from each other, and not syncytial in their nature. They are much more easily damaged by toxic irritants than

are the clear, **flattened cells** lining the descending or narrow part of Henle's loop, and the **clear, cubical** or **columnar cells** of the junctional and collecting tubules and the excretory or uriniferous ducts of Bellini

The **distribution of the blood-vessels** of the kidney is also of great importance pathologically (*see* fig. 390). The **renal artery** divides into four or five **primary branches,** which pass in at the hilus and proceed into the kidney-substance. At the level of the bases of the pyramids, these divide into the **arterial renal arches** (*aa*), which, in turn, give off the **interlobular arteries** (*ai*) to the cortex, and the **arteriolæ rectæ** (*ar*) to the medulla. The **interlobular arteries** (*ai*) pass directly outwards through the cortex between the medullary rays, so that, in a vertical section, these two sets of structures will alternate with each other, forming regular radiating lines in the cortex. The interlobular arteries give off a series of short twigs, the **afferent arterioles,** each passing to a Malpighian body (*g*), in which it breaks up into a little bunch of capillaries which are invaginated into Bowman's capsule, forming the **glomerular tuft** or **glomerulus.** This tuft is loosely covered by a single layer of somewhat polygonal epithelial cells, which are essentially different from the cells lining Bowman's capsule. The capillaries of the tuft become reunited into a single small vessel, the **efferent arteriole,** which emerges near the afferent arteriole. This efferent vessel again breaks up, forming the **intertubular plexus of capillaries** (*ip*), and it may also, if near the boundary zone, send a twig down into the medulla (**pseudarteriolæ rectæ** (*ar'*)). The interlobular capillaries unite into small venules which, together with the stellate veins (*vs*) under the capsule, go to form **interlobular veins** (*vi*). These, in turn, run into the **venous renal arches** (*va*), from which are formed the main **renal veins.** The **arteriolæ rectæ** (*ar*) pass down into the medulla, and divide into leashes or pencils of minute vessels which run down nearly parallel with one another, these " bundles of Ferrein " alternating with the bundles of tubules, and giving the characteristic striated appearance to the pyramids. Corresponding **venulæ rectæ** (*vr*) pass up to join the venous renal arches.

Owing to the presence of the fibrous capsule, especially if it is thickened by disease, profound changes may sometimes be present in the kidney-tissue with little or no alteration in the size and naked-eye appearance of the organ; though, in many instances, both of these are greatly altered. **Microscopical examination** is, therefore, essential for the proper investigation of such specimens, and too much trust should not be put on the naked-eye appearances, though, of course, these may often give very important information as to the nature of the lesions present.

The **naked-eye examination of the kidney,** to be of any value, must be systematic, and should include the observation of such points as its **position, size, shape, weight, consistency, condition of the capsule, surface,** and **sectional appearances** (*see* footnote [1]).

[1] NOTE.—**Systematic Naked-eye Examination of the Kidney :—**
1. **Position,** etc., while still in the body.
2. **Size, shape,** and **weight**—average 8½ to 9 oz. (about 240 to 250 grammes), or about 1/240th of the total weight of the body.
3. **Consistency,** *e. g.* soft and flabby as in fatty degeneration, etc.
4. **Capsule**—**adhesions** to surrounding fat and areolar tissue, and to the kidney itself; **thickening, lamination,** etc., these changes generally pointing to some vascular derangement, the adhesions, etc., being due to establishment of a collateral blood-supply.

Bearing in mind what has been said above with regard to the fact that, as a general rule, no one component tissue-element of kidney can be affected alone without involvement of all, the elementary pathological changes may, for descriptive purposes, be grouped under the following headings :—

A.—Those affecting the Malpighian body and its constituent parts *i. e.* :—

(*a*) The glomerular tuft and its blood-vessels (afferent arteriole, capillaries, and efferent arteriole).

(*b*) The epithelium covering the tuft.

(*c*) Bowman's capsule with its endothelium and connective tissue.

B.—Those affecting the interstitial connective tissue of the kidney.

C.—Those affecting the renal vessels, including arteries, capillaries, and veins.

D.—Those affecting the secreting and uriniferous tubules or glandular tissue proper.

After some of these more elementary lesions have been dealt with, the various degenerative and inflammatory conditions which may be found in this highly complex and delicate organ will be better understood.

5. **Surface** :—
   i. **Smoothness** or **roughness** after stripping capsule, *e. g.* cicatrices, granularity, lobulation, presence of cysts, infarcts, abscesses, tubercles, etc.
   ii. **Colour**—depending largely on condition of superficial veins and capillaries— any engorgement of stellate veins : mottling, pallor.

6. **Vertical Section** :—
   i. **Proportional thickness** of cortex and medulla, and of superficial and inter-pyramidal parts of cortex. Absolute and relative increase or diminution of any of these. Presence of cysts, infarcts, abscesses, tubercles, etc.
   ii. **Differences in colour** in these parts : mottling, etc.
   iii. **Vascularity** of the various parts—depending greatly on the mode of death, presence of heart-disease, etc. Note particularly the condition of vasa recta (especially the veins) running down into medulla, lines of inter-lobular vessels, and glomeruli if these are visible. Presence of hæmorrhages.
   iv. **Regularity** in arrangement of cortex, especially superficial part, shewing alternating lines of tubules and vessels. These should be regular, and not broken up. Presence of cysts. **Condition** of **medullary rays :** presence of "fibromata," etc.
   v. **Ureter, pelvis,** and **calyces**—dilatation, obstruction, presence of calculi, vascularity of mucous membrane, petechial hæmorrhages, etc. Amount of fat in the hilus—often increased in atrophic conditions of the organ.

7. **Condition of renal arteries**—both larger and smaller branches—atheroma, thickening, patency, etc.

8. **Reactions for waxy degeneration** (Iodine): presence of **hæmosiderin** (Prussian-blue reaction), etc.

A.—LESIONS AFFECTING THE MALPIGHIAN BODIES

I. BLOOD-VESSELS

1. FATTY DEGENERATION of the capillary endothelium of the glomerular tufts may be very extreme in cases of phosphorus-poisoning. It may also occur in acute alcohol- and in delayed chloroform-poisoning. In subacute diffuse nephritis, a slight degree of fatty change may be present, and the condition is frequently found as an accompaniment or sequel of waxy degeneration.

2. WAXY or AMYLOID DEGENERATION, in the case of the kidney, is due to the **usual** causes which produce the disease elsewhere, especially **syphilis** and **chronic tuberculosis.** In our opinion, it is never " the result of Bright's disease," as is often erroneously stated. One of us [1] has recorded the occurrence of amyloid degeneration in four cases of chronic heart-disease, in which the usual causes were definitely excluded, and where the only apparent ætiological factor was the poison. of acute rheumatism.

The kidneys may, in rare cases, be the only organs affected; but, much more commonly, there is associated waxy degeneration of the liver, spleen, and perhaps of the intestines and other organs. Waxy disease may be the only lesion present in the affected kidneys, but, very commonly, it leads to, or is associated with, other degenerative or inflammatory conditions, which are brought about either by its interference with the efficient elimination of the toxic products of metabolism, or by the causes which also produce the amyloid change. For this reason, i. e. because of the variations in the associated lesions, in any given instance of waxy disease of the kidneys, the naked-eye and histological appearances of the organs **may vary within very wide limits,** and, for purposes of description, the following four groups of cases may be recognised.

i. **Pure Waxy Disease.**—When amyloid degeneration occurs alone, the kidney may exhibit very slight naked-eye alteration, or there may be a somewhat translucent appearance, especially in the cortex.

ii. **Waxy Disease combined with some other degenerative condition,** especially **fatty degeneration,** and also very commonly with **catarrhal** changes. In such cases, the organ is increased in size, and the glandular tissue is of a dull yellowish-white colour, and, on close inspection, exhibits a finely mottled appearance, due to a mixture of opaque white or yellowish-white fatty areas and the more translucent areas of waxy change proper. This combination with fatty degeneration is what gives the appearance that used to be known as " large white kidney "—a term which is now sometimes applied to an entirely different condition, and is one which we consider it inadvisable to employ.

[1] Beattie, " Rheumatic Fever and Amyloid Degeneration," *Brit. Med. Jour.,* November 24, 1906.

iii. **Waxy Disease combined with interstitial changes.**—This combination of lesions is found especially in syphilis. The kidneys may be considerably enlarged, and may shew marked overgrowth of the interstitial connective tissue.

iv. **Extensive Atrophic Changes** may supervene in organs affected by any of the above-described vascular, catarrhal, or interstitial lesions. The kidney, in such a case, may become small in size, and present an irregular surface closely resembling a "small granular contracted kidney." The size and appearance of the kidney in waxy disease, therefore, depend greatly upon the associated conditions which may be present.

Sequence in which the kidney-structures are most commonly involved. As is usually the case in any given organ or tissue, the disease affects first the "ultimate arterial distribution." In the **cortex,** the change begins usually in the **afferent arteriole** of the **glomerulus,** from which it slowly spreads into the **glomerular capillaries,** the **efferent arteriole** of the glomerulus, the **intertubular capillary network,** the **interlobular veins,** etc., and, at the same time, it spreads backwards to the **interlobular arteries.** It may also come to affect the delicate **connective tissue** and **basement-membranes of the tubules.** In the **medulla,** it begins in the **arteriolæ rectæ,** and may spread to the **supporting connective tissue** between the tubules.

In certain very rare instances, especially in cases of congenital syphilis in children, an exceptional method of distribution may be found, in which the disease is confined to the **interstitial supporting connective tissue between the collecting tubules towards the apices of the Malpighian pyramids.**

The waxy material exhibits the **usual staining reactions** with iodine, methyl violet, etc. (*see* pp. 59–60).

3. HYALINE DEGENERATION is a toxic condition which occurs as the result of the acute action of certain bacterial and other poisons. It is found especially in **scarlet fever** and, to a less extent, in **diphtheria.** It may also occur in some of the more chronic diseases, such as **chronic Bright's disease, chronic lead-poisoning,** etc.

Distribution of the change.—Hyaline degeneration may affect the coats of the **afferent arteriole,** for example in scarlet fever, and may lead to the occurrence of thrombosis within the vessel. In some cases, the degeneration may spread into the **capillaries of the glomerulus** and to the **fine connective tissue** between them, giving the tuft a swollen, homogeneous appearance. It may also extend backwards along the walls of the **afferent arteriole** to the smaller branches of the **interlobular arteries,** especially in some of the more chronic forms, and it may, in some cases, affect the **basement-membrane of Bowman's capsule.** The inner, and also the middle, coats of the arterioles become swollen and present irregular homogeneous masses, which may narrow and even close the lumen, leading to obliteration and fibrous changes in the glomerulus. (For a fuller description of **Hyaline Degeneration,** *see* p. 64.)

II. EPITHELIUM COVERING THE GLOMERULAR TUFT

The pathological changes in this layer of epithelial cells are not so characteristic as those found in the endothelium lining the capsule, the two layers differing from one another, both in their developmental origin and in their pathological reactions. The cells of the former may exhibit **cloudy swelling, fatty degeneration** and similar conditions, usually associated with other glomerular changes.

III. CAPSULE OF MALPIGHIAN BODY (Bowman's Capsule)

The pathological reactions which may occur in the **lining endothelium** and **basement-membrane** of Bowman's capsule, and in the surrounding connective tissue, are of the greatest importance—for example, in sub-acute diffuse nephritis, these reactions are so marked that some forms of this condition have been called **glomerular nephritis,** the changes in the capsule itself having received such names as "capsulitis," "endocapsulitis," "glomerulitis," "periglomerulitis," etc. The reactions usually bring about a thickening or a swelling of the capsule, and may be grouped under three heads. These may occur in varying degree in any given case.

i. **Pericapsular proliferation** and **leucocyte-infiltration**—often most marked round the efferent arteriole or venule.

ii. **Thickening of the capsule itself** is found in subacute diffuse nephritis, especially in scarlatinal cases, and is due to a toxic swelling of the connective-tissue laminae of which the capsule is composed. This change may shew as a clear, homogeneous swelling, or as a fine lamination or infiltration.

iii. **Swelling and proliferation of the endothelial cells lining the capsule.** This is the **most important** alteration—these cells in many ways reacting like **vascular endothelium,** and differing completely from the cells lining the secreting tubules, and from those covering the tuft. They are **mesothelial** in their characters and reactions, and are specially liable to proliferative changes precisely resembling those occurring in the lining endothelium of vessels in the condition of proliferative endarteritis—a progressive laminated thickening at first cellular, but later becoming fibrous in character, which fills up the lumen of the capsule. These changes lead to, and bring about, **adhesion between it and the tuft.** At a later period, the tuft, owing to compression and loss of function, becomes **shrivelled** and **atrophied.** (*See* figs. 391, 399, and 400.)

This **obliteration of the glomeruli** will also affect the **tubules** in the neighbourhood—

(1) By lessening or abolishing the watery secretion from the glomerulus, and so preventing the proper flushing or washing out of the corresponding uriniferous tubule.

(2) By cutting off the blood-supply normally passing through the

glomerulus to the neighbouring part of the cortex by way of the efferent arteriole and intertubular capillaries (see fig. 390).

If these changes take place slowly, a progressive atrophic condition is produced, the epithelium of the tubules becoming smaller, and the cells losing their typical " granular " and striated character, and coming to resemble mere duct epithelium (see fig. 402). A more rapid degeneration of the epithelium results if the glomerular changes are acute. The corresponding interlobular arteries lose their function, and undergo obliterative changes. Small anastomosing vessels then pass in from the surface, causing adhesion and dipping in of the capsule. In the areas
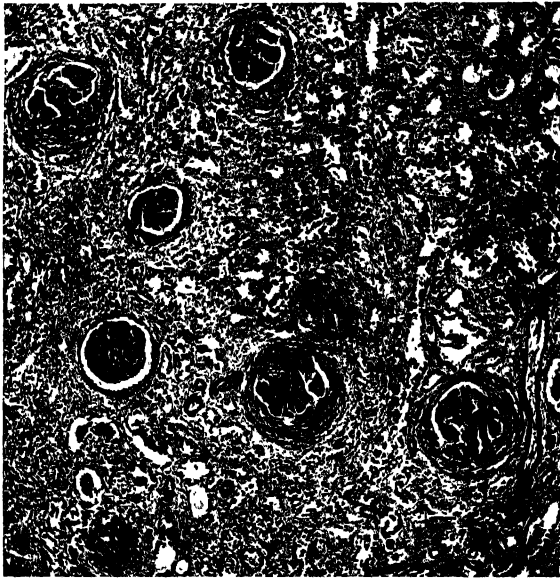
FIG. 391.—*Subacute Interstitial Nephritis*, with marked glomerular changes. The glomeruli shew progressive proliferation of the cells lining Bowman's capsule, and the other changes described in the text. × 50.

of the cortex in which the tubules are degenerating, atrophy and contraction of these structures gradually occur, and may be followed by overgrowth of fibrous tissue. In the intervening areas, the tubules undergo dilatation. Thus, the vascular markings become distorted. These phenomena are best illustrated in one of the forms of granular contracted kidney (see figs. 403 and 405). In the kidneys of old people, small, isolated, rounded, laminated fibrous nodules are often seen microscopically. These are the remains of Malpighian bodies which have undergone a similar degeneration owing to the cutting-off of their blood-supply by senile changes in the vessels. Glomeruli shewing intermediate stages of the process may also be observed, e. g. with laminated thickening of the capsule, shrinking of the tuft, etc.

B.—LESIONS AFFECTING THE INTERSTITIAL CONNECTIVE TISSUE OF THE KIDNEY

The supporting or interstitial connective tissue of the kidney varies greatly in amount in different parts of the organ. It is most abundant in the pyramids, especially towards their apices, whilst in the cortex, between the tubules and glomeruli, it is extremely scanty, and forms a very delicate network between these and the capillaries, lymphatics, etc. It is some-what more plentiful around the vessels; and pathological changes, e. g. pro-liferation, leucocyte-emigration, etc., are, therefore, usually best marked round these, and also round the glomeruli. In some cases, however, there may be a more generalised interstitial overgrowth. Such over-growth is very common in subacute and chronic inflammatory, and in degenerative, conditions, and may occur either primarily, or secondarily to changes in the glomeruli, tubules, or vessels.

C.—LESIONS AFFECTING THE VESSELS OF THE KIDNEY

Changes affecting the vessels of the kidney are highly important, e. g. in relation to regulation of blood-pressure, blood-flow, and excretion of urine; and the vessels are profoundly diseased in almost all cases of chronic renal disease.

(a) **ARTERIES.**—The arteries of the kidney are liable to the ordinary diseases affecting vessels elsewhere. They are specially exposed to conditions of strain from alterations of blood-pressure, which is high during active excretion, and also to damage from the action of soluble toxic substances, normal and abnormal, which it is part of their function to excrete from the blood. **On section,** the larger arteries may stand out prominently and appear abnormally large and dilated (*see* fig. 403), and, on **microscopical examination, end- and peri-arteritis** may be observed, often associated with **fibrous thickening** or, it may be, a true **hyper-trophic condition**—most frequently, perhaps, a combination of **both** fibrous tissue and muscular proliferation—of the middle coat (*see* fig. 392).

In addition to the other recognised factors in their production, **ather-omatous changes** are specially liable to occur where there is local obstruc-tion to the circulation of the blood through the organ, and this may be caused in the kidney-lesions, especially in the vessels, by the **glomerular changes** above described. The atheromatous and the glomerular changes react on one another, and, when once set up, each will tend to aggravate and increase the other.

When excretion by the kidneys becomes defective or deranged, an irritative spasmodic contraction of all the small arteries throughout

the body may be produced, due to the action of some substance or substances of more or less unknown nature, which should be excreted by the kidney, and which, therefore, naturally have very marked local effects on the vessels of the kidney itself.

Acute changes in the cortex have a special tendency to begin **around the inter-lobular vessels near the boundary zone;** whilst most of the **chronic changes** tend rather to begin towards the surface of the kidney, *i. e.* nearer the **terminal distribution of the vessels.**

Hyaline degeneration of the smaller arteries and arterioles has been already mentioned (p. 874), as has also **Waxy Disease** of the renal vessels (p. 873).
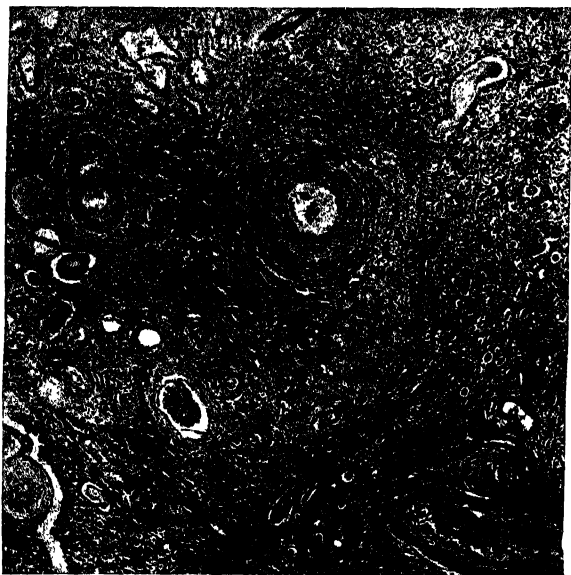
Fig. 392.—*Chronic Granular Contraction of Kidney.* Medium-sized artery, in transverse section, shewing proliferation of intima, and hypertrophy and fibrous thickening of middle coat. There is marked perivascular proliferation of fibrous tissue. × 50.

(*b*) **CAPILLARIES :—**

i. **Of Glomeruli** (already considered on p. 873).

ii. **Inter-tubular Capillary plexus.**—This, as already explained, is specially liable to be affected by **glomerular disease.** The vessels are very intimately connected with the **tubules** which they supply, and between which they run, and therefore are likely to suffer in disease of the tubules— for example, they will be compressed by swelling of the tubular epithelium. They will also be affected by any interstitial proliferation around them, and may become compressed and narrowed to a varying degree in such conditions.

iii. **Vasa Recta and Capillaries of Medulla.**—The arteriolæ rectæ, given off by the arterial renal arches—and to a slight extent from the inter-

lobular arteries and efferent glomerular arterioles near the boundary-zone, *see* fig. 390 (*ar, ar'*), p. 868—pass down into the medulla, and divide into leashes of **straight capillaries** which run between, and supply, the looped tubules, collecting tubules, and uriniferous ducts. These vessels are specially subject to **Waxy Degeneration,** as already indicated, and are also liable to become dilated in cases of **acute,** and more particularly of **chronic, venous congestion.**

(*c*) **VEINS.**—These shew specially the changes described under **chronic venous congestion** (*see* p. 908).

D.—PATHOLOGICAL CONDITIONS AFFECTING ESPECIALLY THE TUBULES OF THE KIDNEY

Degenerative changes may occur very readily in the epithelial cells of the tubules, especially where these are most highly endowed and specialised, *i. e.* in the proximal convoluted tubule, the ascending or broad part of Henle's loop, and, to a less extent, the distal convoluted tubule. Such damage to the epithelium may be due to the **action of bacterial toxins,** *e. g.* in diphtheria, pneumonia, etc.: or of certain **toxic products of metabolism,** such as are produced when renal or hepatic excretion is abnormal, or from other causes. **Poisons,** such as corrosive sublimate and cantharides, may also cause very intense degenerative changes in the renal epithelium, and may lead to extensive necrosis of the more delicate cells.

Any **interference,** either total or partial, sudden or gradual, **with the blood-supply** of the organ, will cause very important degenerative changes. Cutting off of the blood-supply, by means of a ligature, for an hour, will lead to very serious damage; and for an hour and a half, may cause extensive necrosis of the tubular epithelium in the above-mentioned situations. Similar changes may be produced acutely by embolism or thrombosis; or, in a more gradual manner, by chronic vascular diseases such as obliterative endarteritis. In like manner, as mentioned above, any **obliterative lesions of the glomeruli** will affect the tubules, by eliminating or cutting off the blood-flow into the inter-tubular capillaries, and also by interfering with the watery secretion of the glomerular tufts, and thus preventing its normal passage down the corresponding tubules.

(1) **CLOUDY SWELLING OF THE KIDNEY** is an exceedingly common phenomenon, and is produced by the usual causes, as, for example, the action of bacterial and other poisons; and typical specimens of this may be seen after death from pneumonia, diphtheria, typhoid, and various other acute infective fevers. In such cases of cloudy swelling, there may be, clinically, a corresponding, more or less transitory, **albuminuria;** and marked **swelling** of the organ, and a **softening** in its consistence, are usually present. The cortex is swollen, pale, and opaque—as if it had been

dipped in boiling water; and its vascular markings are obscured owing to compression and emptying of the vessels by the swollen tubules, the result being a more homogeneous appearance to the naked eye. In the earlier stages, there is marked congestion, which, for the reason just mentioned, soon passes off, remaining longest in the straight vessels of the pyramids. The red, congested condition gives place first to a pinkish-white, and later to a pale opaque-whitish tint. All degrees of cloudy swelling may occur, and the ultimate results upon the organ will depend, naturally, on the intensity and duration of application of the irritant. If slight in degree, the epithelium may entirely **recover;** or, if more severe, the recovery may be only **partial** and the cells be **degraded to a lower type,**

Fig. 393.—*Cloudy Swelling in Secreting Tubules of Kidney.* The smaller tubules are the narrow portions of Henle's loops, and are less affected than the larger convoluted tubules, which shew swelling of the cells (producing an irregularly stellate lumen), loss of nuclear staining, etc. From a case of acute pneumonia. × 200 diam.

e. g. cubical or even flattened epithelium may replace the columnar type. The cells may undergo secondary **fatty,** or other **degenerative** and **necrotic, changes.** In severe cases, **catarrhal** or other **inflammatory** phenomena may supervene, and these are generally associated with **fatty degeneration.**

(2) **FATTY DEGENERATION.**—Cases of fatty degeneration of the kidney may be divided into two great groups—those in which the condition is **primary,** and those in which it is **secondary,** *i. e.* supervenes upon, and is associated with, other pathological lesions such as cloudy swelling, inflammation, etc.

Primary Fatty Degeneration of the kidney tends to occur in **toxic** and **chronic wasting diseases** such as cancer, phthisis, diabetes, prolonged fevers, etc. It may arise from the action of certain **poisons** such as arsenic, phosphorus, alcohol, chloroform, etc.; or it may be produced

Fig. 394.—*Cloudy Swelling of Secreting Tubules of Kidney.* Shewing the changes described in the text. From a case of typhoid fever. × 300.

(b)   (a)   (b)

Fig. 395.—*Necrosis of Tubules following upon Cloudy Swelling in the Kidney.* Shewing absence of nuclei in the majority of the cells of the secreting tubules. (a) Collecting tubule, least affected. (b) (b) Secreting tubules, most affected. × 300.

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by **deficiency, excess,** or other **abnormalities of nutrition.** Among the last-mentioned causes, diabetes mellitus is very commonly placed, but the fatty changes in this disease are perhaps due also to the action of some as yet unknown **toxic** agent or substance; the same being in all probability the case with regard to fatty degeneration of the kidney in pernicious anæmia.

The fatty change affects especially the highly-organised convoluted secreting tubules and the thick or ascending portion of Henle's loop, the cells of which come to contain large numbers of minute oil- or fat-globules, which are situated especially in the outer parts of the cells towards the basement-membrane (*see* Plate I, fig. 2). These granules,
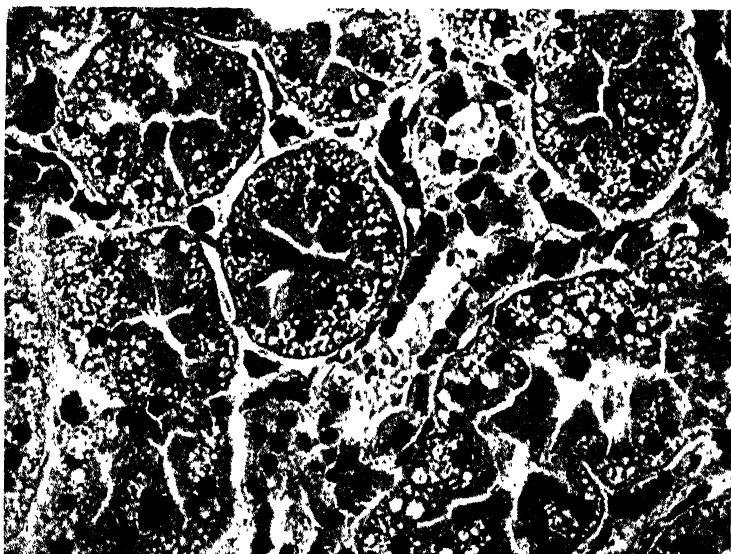
FIG. 396.—*Fatty Degeneration of Epithelial Cells of Convoluted Tubules of Kidney.* The clear areas represent the position of the fat, removed during the process of paraffin-embedding. The cells also shew cloudy swelling. × 450.

as a rule, remain small and discrete, but, in some of the more intensely acute cases, *e. g.* in **delayed chloroform-poisoning,** they may attain a somewhat larger size and undergo a certain degree of coalescence. In severe cases, the endothelial cells of the capillaries, both intertubular and glomerular, may also be affected. The epithelial cells of the collecting tubules and other less highly differentiated structures suffer to a much less degree.

Secondary Fatty Degeneration.—The association of fatty degeneration with **cloudy swelling,** and its relation to the latter condition, of which it **may** be a sequel, are fully discussed in Chapter II, pp. 30 and 33. Fatty degeneration may also occur, and be associated, with **catarrhal** and **inflammatory** changes, and with **waxy** or **amyloid degeneration.** In such cases, the process may be extensive, and is usually irregularly distributed

in patches, giving a yellowish or yellowish-white, finely-mottled appearance to the cut surface, some parts being more markedly affected than others. In these secondary forms of fatty degeneration, the fat-globules may be larger in size than in the primary forms. Relatively large globules may thus be found in catarrhal cells which have become detached from their basement-membrane and are lying free in the lumen of the tubules (*see under* **Nephritis,** pp. 889, 891, etc.).

(3) **MUCOID AND COLLOID (MUCINOID) DEGENERATION.—** Damaged epithelial cells, either *in situ* or after separation from their basement-membrane, may absorb lymph or some of its albuminous constituents. These swollen cells, together with transuded leucocytes, etc., may fuse to form what are called " **casts** " in the tubules. These processes of cast-formation occur both in chronic degenerative conditions, and in acute, subacute, or chronic inflammations.

(4) **THE OCCURRENCE OF " CASTS " IN RENAL DISEASE.** --Collections of solid or semi-solid material, *e. g.* cells, fibrin, etc., may fill the tubules, and form cylindrical casts in them. These casts may be seen, microscopically, *in situ*, in sections of the kidney, or they may be found in the urine. In the latter case, they are formed probably in the segment of the uriniferous tubule extending from the termination of the ascending part of the loop to the opening of the excretory tube at the apex of the papillæ—most commonly in the straight or collecting tubules, from which they can be easily washed out into the urine. It is practically an impossibility for casts formed in the convoluted tubules to be carried as such through the descending loop of Henle and the other narrow portions of the tubular system (*see* fig. 390), though one not infrequently meets with descriptions of their alleged occurrence in the urine.

Varieties of Casts :—

1. **Those composed of altered tubular epithelium :**
   i. **Epithelial casts,** formed of desquamated epithelial cells, which are often mixed with leucocytes, fibrin, etc. These may undergo various degenerative changes, and be found as—
   ii. **Colloid casts** (sometimes wrongly called " waxy "). When swollen, clear, and homogeneous-looking, these form one variety of **hyaline casts.**
   iii. **Granular casts,** where the cells are undergoing granular disintegration.
   iv. **Fatty casts,** where they shew fatty changes.
2. **Those composed of altered blood or inflammatory exudate :**
   i. **Blood-casts,** of altered or unaltered red blood-corpuscles.
   ii. **Leucocyte-casts.**
   iii. **Fibrinous and albuminous casts,**—another variety of the so-called **hyaline casts** (*cf.* 1, ii).

iv. **Blood-pigment casts,** containing granules or crystals of altered hæmoglobin (hæmatoidin, etc.).

3. **Those composed of normal or abnormal urinary constituents, or other substances excreted by the kidney :**

i. **Urates, uric acid,** etc.

ii. **Bile-pigment,** *e. g.* bilirubin, in some long-standing cases of jaundice.

iii. **Calcareous casts.**—Calcification may occur in necrotic epithelial and other forms of casts.

INFLAMMATORY CONDITIONS OF THE KIDNEY

I. **SUPPURATIVE NEPHRITIS.**—**Pyogenetic bacteria** may find their way to the kidneys by means of the **blood-vessels,** the **lymphatics,** the **urinary passages,** or, directly, by **traumatic** lesions. In **ulcerative endocarditis or** in **pyæmia** from other causes, **minute abscesses** may occur in the kidney-substance, owing to the impaction of small **septic emboli,** originating from a breaking-down septic thrombus in a vein, or from an infective vegetation on one of the heart-valves. These abscesses may be found throughout the kidney-substance, but, owing to the fact that the emboli are usually small in size and tend to be caught in the smaller branches of the arteries and in the glomerular and intertubular capillaries, they are found especially **along the lines of the vessels** in the cortex, frequently exhibiting a radial appearance corresponding to the distribution of those vessels. They may also be found along the arteriolæ rectæ in the medulla, and even around some of the larger branches of the renal artery. **On microscopical examination,** a minute thrombosed artery or capillary, containing a dark-staining plug of organisms, most commonly *Staphylo-* or *Strepto-cocci,* can usually be found in the centre of such an embolic abscess (*see* fig. 397). Around this little vessel, if the embolism has occurred a sufficient length of time before death, intense necrotic changes may be seen in the neighbouring kidney-tissue, the structural characters of which become lost. The necrotic area shews diffuse staining with the acid dye (*e. g.* eosin), and an infiltration with leucocytes, chiefly of the polymorphonuclear type. At a later period, softening supervenes, and minute abscesses are formed, which tend to be elongated in the line of the vessel in which the condition originates. Neighbouring abscesses may coalesce, giving rise to lines of more diffuse suppuration. When the septic emboli have become impacted only a short time before death, plugs of micrococci may be found in some of the vessels, with very little or no inflammatory reaction around them.

Another and very common variety of suppurative nephritis is that due to the spread of infection **from below,** by way of the urinary passages or by their lymphatic channels. This condition has been variously

denominated " **consecutive nephritis,**" " **surgical kidney,**" or, from the fact that the pelvis is involved as well as the substance of the kidney, **suppurative pyelo-nephritis.** The second of these terms arose from the great frequency with which the condition supervened upon surgical interference with the urinary passages—especially the use of the catheter —in the days before asepsis was understood and practised. This form of suppurative nephritis is specially common in conditions which produce or lead to cystitis: for example, paralysis of the bladder in lesions of the spinal cord, the irritation of calculi, gonorrhœal infection, the passage of a dirty catheter, etc. The kidney is generally infected by-the spread of
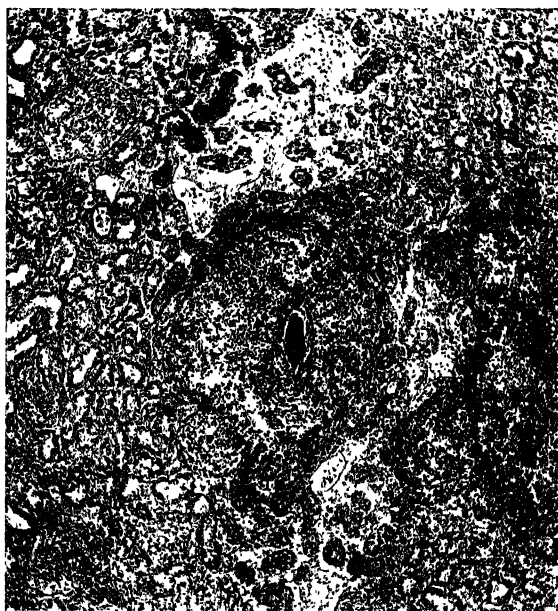
Fig. 397.   *Abscess in the Kidney.* Shewing darkly-stained central embolic plug of bacteria in a small artery, with surrounding mass of leucocytes.   × 50.

a catarrhal change up the ureter to the pelvis. In the latter, the earliest naked-eye manifestation of the inflammation is usually found in the little pouches where the calyces surround the papillæ. A suppurative pyelitis may develop, and this may spread to the kidney substance and become a **pyelo-nephritis.** In some cases, the condition starts in the pelvis of the kidney itself, *e. g.* when it is the seat of calculus-formation. The exact route by which the infection reaches the kidney-tissue is still doubtful. There are three available channels of infection, viz. the blood-vessels, the lymphatics, and the uriniferous tubules—the last being in all probability the least common route. The minute abscesses characteristic of the condition are distributed **along the lines of the vessels,** but it is uncertain whether the condition is due to embolic infection by way of the blood-vessels, as is the case in ulcerative endocarditis and in pyæmia, or to a

spread by way of the lymphatic channels situated in the connective-tissue framework of the kidney, and which are specially numerous around the vessels.

The **naked-eye** appearances of the kidney are, as a general rule, very characteristic. The organ is usually swollen, softer, and more vascular than normal. On the surface beneath the capsule, and along the lines of the vessels in the substance of the organ, are seen small, whitish or yellow-ish-white points, arranged singly or in clusters, each surrounded by a zone of intense hyperæmia. These are scattered irregularly along the lines of the vessels, both in the medulla and in the cortex, forming dotted, radiating lines, which may sometimes extend from the apex of a papilla to the surface of the kidney. **Both** organs are usually affected, though often in varying degree; and, associated with the condition, there is always intense catarrh of the pelvis and of its calyces **(pyelitis)**—this being usually most marked immediately around the papillæ of the Malpighian pyramids.

Traumatic suppuration of the kidney may occur, especially where there is rupture of the renal substance or of a cyst.

PYELITIS OR INFLAMMATION OF THE PELVIS OF THE KIDNEY. This condition may be **suppurative** or **non-suppurative.** Milder degrees of pyelitis may be due to the excretion by the kidney of irritants such as cantharides, turpentine, sandalwood, copaiba, etc.: or to acute retention, chronic urinary obstruction, etc. Pyelitis arises most usually by direct spread of infection from the kidney-tissue above, or from the bladder and ureter below, though occasionally it is due to direct hæmatogenous infection. Bacteria may pass into the blood-stream from a tonsillitis, boil, carbuncle, pyorrhœa, or some other local infective conditions: or through the intestinal mucous membrane in constipation, catarrh, etc. In typhoid, paratyphoid, Mediterranean, and other infective fevers, the causal organisms are practically always present in the blood at some stage of the disease. Such organisms are removed from the blood by the liver and kidneys. In the case of the kidney, little local damage may follow, but, on the other hand, a pyelitis or pyelo-nephritis may be produced. It may occur in either sex and from a large number of infective causes, but it is particularly common in the female immediately after marriage, during pregnancy, or after parturition, and is very frequently due to infection with *B. coli.* Acute pyelitis is not at all uncommon in infancy and early childhood, especially in girls, and is usually associated with intestinal trouble, especially constipation, or constipation with occasional attacks of diarrhœa. The commonest organism found in these cases is *B. coli,* though *staphylo-* or *strepto-cocci* [1]

[1] The group of *Streptococci* associated with acute rheumatism, and chronic rheumatic, rheumatoid, and allied conditions, are excreted with great frequency in the urine, usually with little or no local evidence, as judged merely from examina-tion of the urine, of any active inflammatory or other reaction in the genito-urinary system itself.

may occur, and the authors have also not infrequently found *B. para-typhosus*. In certain cases, however, pyelitis may arise from some cause in the pelvis itself, most commonly from the irritation of a calculus or calculi, or of oxalate-crystals, etc., with secondary bacterial infection.

If suppuration is produced, and the pelvis of the kidney becomes distended with the pus so formed, the term **pyo-nephrosis** is applied to the condition. As a result of this pyo-nephrosis, which may also be caused by suppuration supervening in a case of hydro-nephrosis (*q.v.*, p. 906), the kidney becomes progressively destroyed—owing partly to pressure, and partly to an extension of the suppurative process into it—and may ultimately be represented by a sacculated bag of pus, the walls of which are formed by the distended pelvis and the capsule of the organ. The condition, in some cases, especially if both kidneys are involved, causes the death of the patient, but, in others, where only one organ is affected, the pus may become inspissated by absorption of its fluid constituents, leaving as a residue a white, or yellowish-white, plaster-like mass, in which calcification is liable to occur. In such a case, it is sometimes difficult to determine whether the condition has originally been due to suppurative organisms or to tuberculosis.

PERI-NEPHRITIS, PERI-NEPHRIC AND PERI-NEPHRITIC ABSCESS.
Inflammation of the tissues immediately around the kidney may be **suppurative** or **non-suppurative.** In the latter case, the condition may become chronic and lead to **fibrosis** of the fatty tissue around the organ, with adhesions to the capsule. The kidney is usually itself diseased in such cases, and any form of chronic inflammation such as pyelo-nephritis, pyo-nephrosis, calculus, tuberculosis, etc., may be found. Lesser degrees of fibrosis of the peri-nephric fat may be due to vascular changes secondary to those in the kidney, described on pp. 876 and 896–7. On the other hand, suppuration may occur in the loose fatty areolar tissue around the kidney. The latter may thus become embedded in an abscess, the substance of the organ itself, unless previously involved, remaining, as a rule, free from the suppurative process. The condition may be due to the rupture of a cyst on the surface of the organ, or to the extension of an infective process in the pelvis or some other part of the kidney; but, in many instances, the cause lies altogether outside the kidney itself. Thus, it occasionally arises during the course of some infective fever, such as typhoid, scarlet fever, measles, pneumonia, etc., or as a complication of tonsillitis, carbuncle, etc.; or it may be due to the extension of some infective condition from neighbouring parts, *e. g.* from tuberculous or other disease of the vertebræ or lower ribs, from an empyema burrowing downwards, or from the extension of an abscess in connection with the intestines or other abdominal viscera. In many cases, however, the cause is obscure. The commonest organisms found are, in order of frequency, *B. coli* or organisms of coliform type, *Strepto-* and *Staphylo- cocci, Friedländer's bacillus,* and, much more rarely of the *Pneumo-* and *Gono- coccus.*

II. **NON-SUPPURATIVE NEPHRITIS.**—Various forms of inflammatory disease of the kidney are often included under the name " Bright's Disease," which, however, is a very indefinite and loosely-applied term. **Bright's Disease** usually signifies a morbid condition of the kidney accompanied clinically by albuminuria, and includes some **inflammatory** conditions, some **non-inflammatory** chronic degenerative changes, and frequently **mixtures of both.** With the albuminuria, there may be associated in some cases **dropsy,** in others **uræmic symptoms,** and in others both of these conditions.

On the other hand, uræmia may sometimes be found—especially in certain cases of granular contracted kidney—without albuminuria.

Varieties of Nephritis.—Nephritis may be **acute, subacute,** or **chronic;** and, frequently, **combinations of these various forms** are found in the same organ—acute or subacute exacerbations being of frequent occurrence in kidneys which are already the subject of chronic inflammatory and degenerative lesions. The **cause** of non-suppurative nephritis is commonly the action of some **toxic irritant** carried to the kidney by the blood-stream : for example, the bacterial or other toxins produced in diphtheria, scarlet fever, pneumonia, and other acute infective fevers and septicæmias.

Under the term " **Trench Nephritis,**" of which so many cases were described during the war, it is probable that a number of different conditions is embraced. Many cases so diagnosed have been simply a nephritis of any of the ordinary recognised types, occurring in soldiers exposed to severe climatic, and other predisposing conditions; but, excluding these, a considerable number of cases have occurred in which some more specific infective agent appears to be the cause. This subject will be dealt with on p. 904. In other cases, the kidney-lesions appear to be due to the action, often over prolonged periods, of **normal** or of **abnormal products of metabolism.** The usual example cited of this is the form of nephritis occurring in gout, but it is by no means improbable that here also we are dealing with the effects of a chronic infective process. The kidney is extremely liable to the action of **poisonous substances** such as cantharides, turpentine, corrosive sublimate, carbolic acid and its allies, etc. Some of these possess a specially **selective action** upon such parts or elements of the kidney structure as the glomeruli, the secreting tubules, etc.—that is, on parts specially concerned in the elimination of these substances from the system.

Two of the most essential facts to be borne in mind in connection with these forms of nephritis, and to which attention has already been drawn, are, (1) that **both** kidneys are always affected, though sometimes in varying degree; and (2) that their **whole structure**—glomeruli, tubules, interstitial tissue, and blood-vessels—is affected throughout, though in each individual case some of these structural elements may be more specially affected than the others.

A. ACUTE NEPHRITIS.—Acute inflammation of the kidneys may occur in some of the acute infective diseases, especially in diphtheria and scarlet fever, and in cases of poisoning with turpentine, cantharides, corrosive sublimate, etc.

Vascular changes.—These consist of acute hyperæmia with swelling of the organ, and are sometimes very intense. Their development is impeded by the firmness of the capsule, though in a day or two the kidney may increase to two or three times its normal size. In the **glomeruli,** the change is characterised by hyperæmia and hyaline swelling of the capillaries, exudation, leucocyte-infiltration, and perhaps hæmorrhage from ruptured capillaries. In some cases, e. g. in corrosive-sublimate poisoning, there is swelling of Bowman's capsule and swelling and proliferation of its lining cells, but these changes are usually slight. The **intertubular capillary plexus** is engorged at first, but speedily becomes compressed and emptied of blood by the swelling of the tubules. **Acute changes in the walls of the vessels,** such as hyaline degeneration, etc., may be found, and there is usually **engorgement of the straight venules,** around which there may be exudation, leucocyte-emigration, and hæmorrhage.

Intertubular or interstitial changes.—**Lymph-transudation** into the tissues is comparatively slight, except in some septic cases. It is usually seen first round the vessels and glomeruli, forming clearer areas where the tissues are separated; but this change is seldom very marked, probably owing to the firm fibrous capsule of the organ. Lymph-transudation between the tubules is only very slight in amount. **Leucocyte-emigration** may shew specially around the small venules, e. g. the efferent vessels of the glomeruli and the straight venules, and also under the capsule. It is usually only slight, but in septic cases it may be abundant. Many of the emigrated leucocytes, both polymorphonuclear and mononuclear—the latter being often specially numerous—pass into the tubules and assist in the formation of casts. They may exhibit phagocytic activities, or may themselves be taken up by the epithelial cells. Proliferation of connective tissue between the tubules is not pronounced in the early acute cases, and, if at all marked, points to the condition being subacute or chronic rather than acute.

The **epithelium,** especially of the convoluted tubules and the ascending part of Henle's loop, usually shews well-marked degenerative changes —cloudy swelling, granular disintegration, loosening of the cement-substance, catarrhal and necrotic changes, secondary fatty degeneration, formation of casts, etc. These changes in the tubular epithelium are due to the direct action of the toxins on the cells : and also to interference with their vascular supply. Catarrhal and proliferative changes are often best seen in the portions of the uriniferous tubules which are less highly specialised, i. e. in the collecting tubules—hence **casts** are specially liable to be found in the urine in these cases—cellular or forms derived from

these, blood- or blood-pigment casts in hæmorrhagic cases, along with albumin, blood, etc.

Naked-eye appearance of the Kidney in Acute Nephritis.—The kidney is enlarged, soft, and often more rounded than normal. Its capsule is tightly stretched, not thickened in uncomplicated cases, and strips easily, leaving a smooth, pale, mottled surface, upon which the stellate veins are often well marked. **On section,** the cortex, both superficial and deep, is swollen, pale, and mottled. It is sometimes pinkish in colour, and, in intensely toxic cases, may present a uniform or mottled red colour with hæmorrhages. The medulla is usually not much altered, but, in some cases, it shews congestion.

Results.—There may be more or less complete recovery; or, in some cases, the condition becomes subacute or chronic.

B. SUBACUTE DIFFUSE NEPHRITIS.—In some instances, this condition **may** follow a **previous acute attack,** for example, as a sequel of scarlet fever. There is, in many cases, however, no evidence of any such previous acute attack, the disease being apparently **subacute from the first,** with insidious onset and slow progressive course. Some cases appear to follow endocarditis and other rheumatic conditions (*see* footnote on p. 886), pregnancy complicated by albuminuria, etc., and seem to be due to some slow-acting, toxic substance or substances of unknown nature. In all probability a proportion of these cases are produced by chronic infections of the tonsils, throat, gums and tooth-sockets, nasal accessory sinuses, intestine, etc., in which various streptococci and other organisms play an important part. Similar changes in the kidney may be found accompanying syphilitic disease and waxy degeneration, whether the latter, in a given case, be due to syphilis or to some other cause.

The **duration** of such cases varies very much. In **scarlatinal nephritis,** the patient may die during the acute stage, but, more commonly, not till the disease has become subacute, *e. g.* from three or four weeks up to many months after the onset of the fever. Again, the condition may become more chronic, and may last from two to six or seven years—in which case, the condition of the kidneys may come to resemble that found in chronic granular contraction, with fibrous-tissue overgrowth, adhesion of the capsule, thickening of the vessels, and atrophy of the secreting structures.

Naked-eye appearances.—These vary with the cause, duration, and distribution of the change in the kidney. In **early cases,** *e. g.* in those in which death takes place in the course of a few weeks, the kidneys are enlarged from swelling of the cortex; but, in **later cases,** *e. g.* those lasting, say, from seven to fourteen weeks, the enlargement may be slight or absent, or the organ may be normal or even diminished in size, and is generally rather firm in consistence. The capsule is not usually thickened or adherent, and strips readily, leaving a smooth surface, which is

pale or somewhat pinkish in colour, often with numerous small red or brownish-red points upon it. There are usually no cysts. In the later cases (seven to fourteen weeks), the swelling of the cortex may have passed off, especially that in the superficial cortex. This occurs usually where the glomeruli are affected, and where, in consequence, interference with the blood-supply and atrophy of the cortex take place. In such cases, well-marked interstitial changes are generally present. The inter-pyramidal or deep cortex may still shew considerable swelling, as the changes there are often not so advanced as in the superficial cortex, and there is, therefore, in this region, more glandular tissue surviving, in which such swelling may occur. The cortex is usually pale, and often shews a mottled, white or yellowish-white appearance from patches of catarrh and fatty change in the tubules. The lines of the vessels are usually distinct, and shew no distortion, the glomeruli or their vessels being often unusually well seen. Frequently there are also numerous small red or brownish-red points due to dilated vessels, and, in some cases, where the superficial cortex is much diminished, the deep cortex may shew very great swelling and more acute changes, often with well-marked "bran-like" mottling. Where there is any great degree of interstitial overgrowth, the kidney is usually large, firm in consistence, and pale in colour, one form of the so-called "large white kidney"—a term which, as already indicated, it is very inadvisable to employ—often erroneously described as "fatty." Secondary fatty change **may,** however, sometimes be found to a high degree, following upon catarrh of the tubules, and giving rise to the already mentioned mottling of the cortex.

Microscopical examination.—A kidney which may appear almost normal to the naked eye, may, under the microscope, shew **all** its structural elements affected, though, in some instances, the changes in the **interstitial tissue,** and, in others, those in the **glomeruli,** may markedly preponderate.

Vascular changes.—In some early cases, the vessels may not be much thickened, but, even where they appear almost normal to the naked eye, they may be found extensively altered when examined microscopically. In cases of longer duration, there is often very considerable thickening, both of the larger and of the smaller arteries. All the coats may be diseased, and the lumen may be much diminished. The **inner coat** is almost always affected, and may shew cellular and fibrous thickening. The **middle coat** is usually thickened—often very considerably—from actual hypertrophy of its muscular, as well as from overgrowth of its fibrous, tissue. Later, the fibrous changes tend to become more marked, and be accompanied by atrophy and degeneration of the muscle. The **outer coat** may shew very extensive peri-arteritic changes, e. g. fibrous thickening extending into the surrounding tissues, leucocyte-infiltration, etc. Hyaline changes (to which reference has already been made on p. 874), are often present in the smaller vessels, for example, in arterioles and capillaries, especially in those of the glomeruli.

Glomeruli.—The pathological changes in these are of the very greatest importance; and all stages, from swelling of the tuft up to complete fibrous atrophy, may be found in the same kidney. These stages have already been described (p. 875), the most important being :—

i. **Swelling of the tuft from—**

 (a) Engorgement of the capillaries with blood.

 (b) Thickening of the capillary walls from swelling or proliferation of their endothelium, and of their delicate perithelial or supporting connective-tissue coat. The capillary wall may shew hyaline degeneration.

 (c) Swelling and proliferation of the connective tissue between the capillaries.
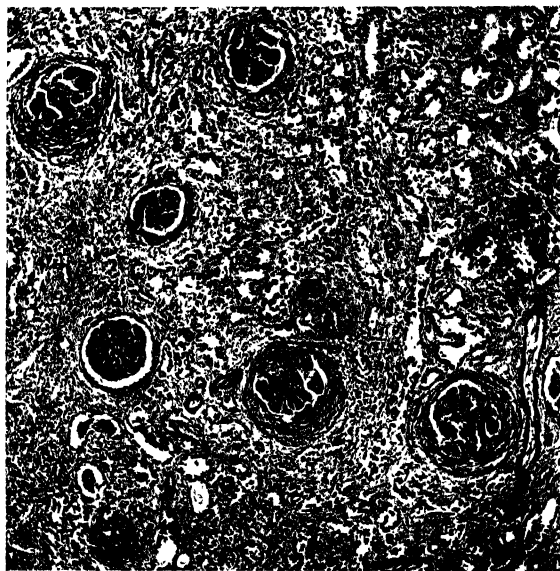
Fig. 398.—*Subacute Diffuse Nephritis*, in which the glomeruli are specially affected, and exhibit the various stages of swelling, proliferation, and obliteration, described in the text. × 50.

 (d) Infiltration of leucocytes between the capillaries of the tuft, inflammatory œdema, and, more rarely, hæmorrhages from the capillaries in the same position.

 (e) Cloudy swelling of the epithelial cells covering the tuft.

ii. **Irregular lobulation of the tuft** (*see* figs. 398 and 399).

iii. **Exudation into the lumen of the capsule** of leucocytes, fibrin, hæmorrhages, etc.

iv. **Swelling of the cells lining the capsule,** usually with proliferation and a progressive, fibrous, laminated thickening, gradually filling up the lumen from the capsule inwards (*see* fig. 399).

FIG. 399.—*Subacute Diffuse Nephritis.* Glomerulus shewing lobulation of tuft, proliferation of endothelium lining Bowman's capsule, and progressive obliteration of lumen.   × 200.

FIG. 400.—*Subacute Diffuse Nephritis.* Glomerulus shewing more advanced changes—Adhesion of the layers of proliferated endothelium to the tuft, with obliteration of the lumen, and progressive fibrous atrophy of the tuft.   × 200.

v. **Adhesion** of these proliferated endothelial cells, etc., to the tuft, and obliteration of the lumen of Bowman's capsule, and hence abolition of the function of the glomerulus.

vi. **Consequent progressive fibrous atrophy of the glomerulus,** with obliteration of its capillaries, and gradual shrinking, until nothing is left but a small, rounded, laminated, fibrous scar (see figs. 400 and 406).   •

vii. **Around the glomeruli** there may be exudation, leucocyte-emigration, proliferation of connective tissue. etc. In many forms of subacute nephritis, these glomerular and peri-glomerular conditions are the most important changes present. They are found especially in scarlatinal nephritis.
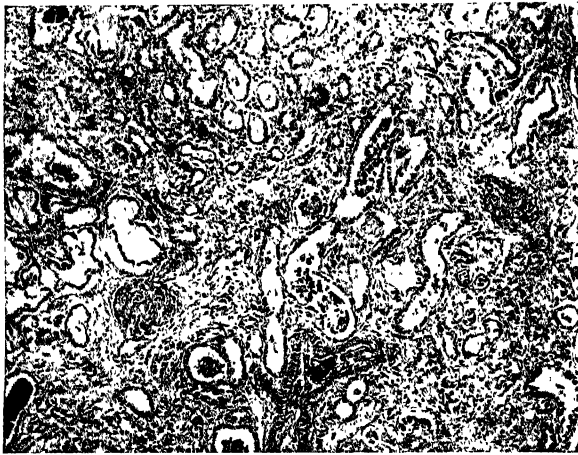
Fig. 401.—*Subacute Diffuse Nephritis* with special increase of interstitial tissue—sometimes called "Interstitial Nephritis." × 75.

Interstitial changes.—The interstitial tissue between the tubules, and particularly round the glomeruli and vessels, may shew various degrees of proliferation, sometimes more cellular, sometimes more fibrous, in its characters (see figs. 400, 401, and 402). Infiltration with mononuclear leucocytes, mostly small lymphocyte-like cells, and other inflammatory changes, as above mentioned, are often specially marked around the glomeruli and vessels, and also sometimes immediately subjacent to the capsule of the organ. In certain cases, this interstitial overgrowth may be very marked, the change in the large pale kidney being, as mentioned above, sometimes mistaken for fatty degeneration.

Epithelium of the Tubules.—The convoluted tubules are abnormally separated from one another by the above-described interstitial changes (see figs. 398, 400, 401, and 402). Pathological alterations in the tubules are usually not uniformly distributed, e.g. some shew swelling of their epithelium, catarrh, and fatty changes; others appear shrunken and

smaller than normal; others dilated, and with their epithelium atrophied and degraded to a lower type; whilst others again may be filled with various forms of casts. Casts are also seen in the collecting tubules, and may pass into, and be found in, the urine, along with numerous single cells and leucocytes. These changes are due, firstly, to **obliteration of the glomeruli,** with consequent stoppage of their watery secretion and cutting off of some of the blood-supply to the tubules; and, in the second place, to the **direct actions of the toxins** on the cells themselves.

The naked-eye and microscopical changes in such a kidney may be
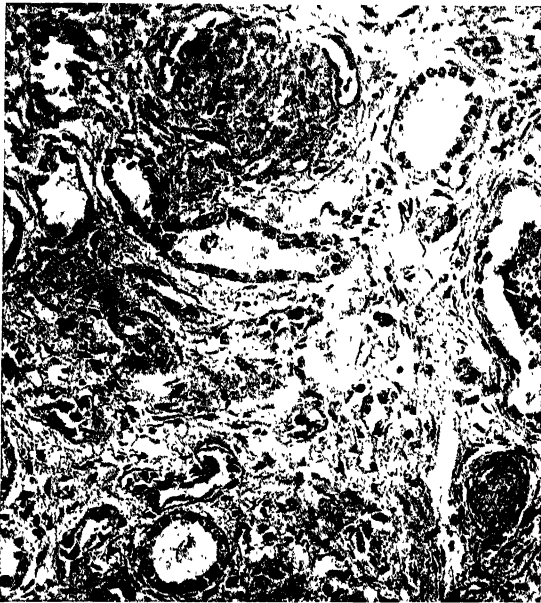
Fig. 402.—*Subacute Diffuse Nephritis* with marked interstitial overgrowth; glomerular changes (*g. g.*); separation of tubules, the epithelium of which shews changes described in text. × 200.

further complicated by the occurrence of a superadded **more acute exacerbation;** by the presence, in some cases, of concurrent **waxy disease;** and by the addition of further advanced and more **chronic changes,** from the supervention of which the condition may gradually come to resemble that seen in chronic granular contraction.

C. CHRONIC GRANULAR CONTRACTED OR CIRRHOTIC KIDNEY.

The term " **granular** " was originally applied by Bright to the **mottled appearance** of the cortex, seen **on section** of the kidney, in cases of dropsy accompanied by albuminuria. Thus, he spoke of the " large pale granular " kidney, " contracted granular " kidney, etc. At the present day, however, the term has come to be applied rather to the character of the **surface** of the organ, especially in certain chronic cases accompanied by

contraction, or by the processes preceding and leading to it (*see* figs. 403 and 407).

Three varieties of chronic granular contraction may be distinguished, but it is impossible to give an absolutely hard and fast classification, as all intermediate forms between the extremes may be seen, and, in a given case, in addition to the characteristic chronic changes, there may be superadded secondary more acute and subacute processes. All intermediate forms may also be found between the subacute varieties of nephritis, described above, and the chronic condition now under discussion.

These three main types of **Chronic Granular Contracted Kidney** are : (i) The **small red granular contracted kidney**—(Atrophic or Arteriosclerotic Kidney); (ii) the **large pale granular " contracting " kidney,** secondary to acute, or more commonly to subacute, nephritis, progressing, later, to further degeneration and atrophy, and becoming (iii) the **small pale granular contracted kidney,** in many cases indistinguishable from the first variety above mentioned.

Various immediate forms may also be found, such as a large red granular kidney, but the colour-distinctions are **not** really of much value, as, amongst other factors, they depend largely on the conditions of the circulation at and preceding death, *e. g.* the presence of chronic venous congestion, hypostatic congestion, etc.

It is impossible to give a single detailed description which will suit each variety of granular contracted kidney, but there are certain characteristics which may be common to all, though, in individual instances, they vary greatly with regard to the size, shape, colour, etc., of the organ. The **capsule** is usually thickened, and adherent both to the surrounding peri-nephric fat and to the surface of the kidney itself. It may strip incompletely and in layers, or fragments of kidney substance may be torn off along with it. The **subjacent surface** of the organ is more or less finely granular or uneven, from the presence of small, rounded, morocco-leather-like projections (*see* figs. 403 and 407). These are more or less regular and uniform in size and shape, but are often associated with deeper furrows and irregularities. Upon it there are usually scattered a varying number of **cysts** of different sizes, from those scarcely visible to the naked eye up to some of comparatively large size (fig. 407). The **superficial cortex** is relatively decreased in thickness, and its vascular markings are extremely distorted and broken up, the normal alternation of the regular lines of vessels and of the medullary rays of tubules being lost. The **deep cortex** may be atrophied, but is relatively more abundant than the superficial. Sometimes it is but little altered in size, and, in other instances, it may even be more swollen than normal, and exhibit a pale, mottled appearance more like that seen in subacute cases, *i. e.* the atrophic changes are more advanced in the superficial, and less so in the interpyramidal, cortex. In the latter position, the disease may, therefore,

be relatively more acute. The undamaged, or partially damaged, tubules, glomeruli, etc., in the deeper and interpyramidal parts of the cortex may become involved in subsequent attacks, and the clinical picture of Acute Bright's Disease be produced in a patient whose kidneys shew mainly a subacute or a chronic lesion. The **medulla** may present little change to the naked eye, or it may also be atrophied. The **blood-vessels** are usually much thickened, and their lumen diminished, the larger arteries commonly shewing well-marked atheroma (*see* fig. 403). Owing to the shrinkage of the whole kidney-substance, there is usually a marked increase of **fat** in the hilus round the pelvis. In vertical section, in many advanced cases, the actual kidney-tissue is represented by a narrow semicircular

A   B   C   D
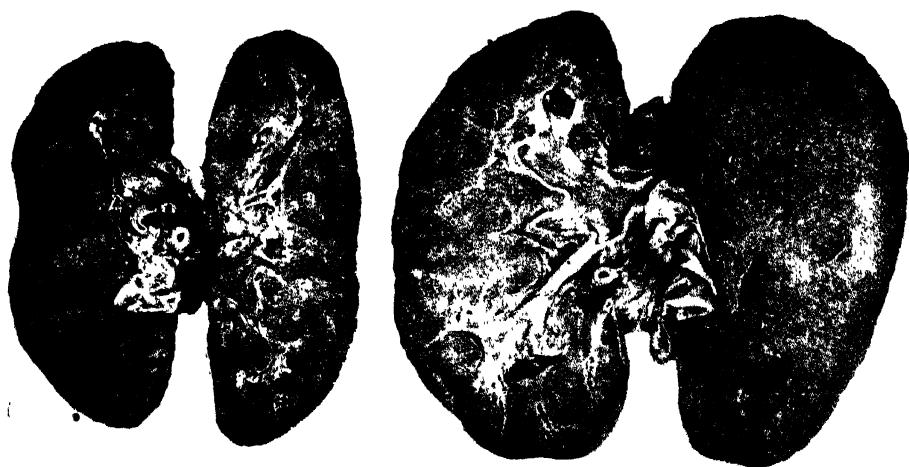
Fig. 403.—*Chronic Granular Contraction of Kidney* (both organs from same case). Type, Small Red Granular Contracted or Arterio-Sclerotic Kidney, the vascular and atrophic changes being more extreme in the left of the two specimens.

A and D, outer surface from which capsule has been somewhat imperfectly stripped, owing to thickening and adhesion. B and C, Vertical section. × ⅞.

rim surrounding this fat; though, in other instances, the fat may be scanty, and the kidney-tissue contracted upon, and closely applied to, the pelvis. On **external** examination of the organ in the former of these, *i. e.* where there is excess of fat in the hilus, the **apparently** larger size of the organ may, therefore, be somewhat misleading, the amount of atrophy being often much more extreme than might be expected from the mere external appearance of the organ. The anastomosing vessels of the pelvis and of the pelvic fat, as well as those of the capsule, take part in establishing a collateral supply of blood to the atrophying kidney.

After the above general synopsis, a more detailed description of some forms of granular contracted kidney may now be given.

i. **Small Red Granular Contracted Kidney,** due to atrophy from **arterial**

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degeneration and consequent diminution in the blood-supply of the organ—sometimes called **Arterio-sclerotic Kidney** (*see* fig. 403). This is essentially an atrophic condition, and the disease commences in the **vessels** and **glomeruli,** especially near the surface of the organ at the terminal distribution of the interlobular arteries. There are progressive fibrous atrophy and obliteration of these vessels, with consequent degeneration and atrophy of the adjacent tubules, as already described when dealing with the elementary lesions of the kidney (*see* fig. 404). As the process advances, more and more glomeruli are destroyed, and, consequently, the corresponding areas of cortex undergo atrophy and shrinking.
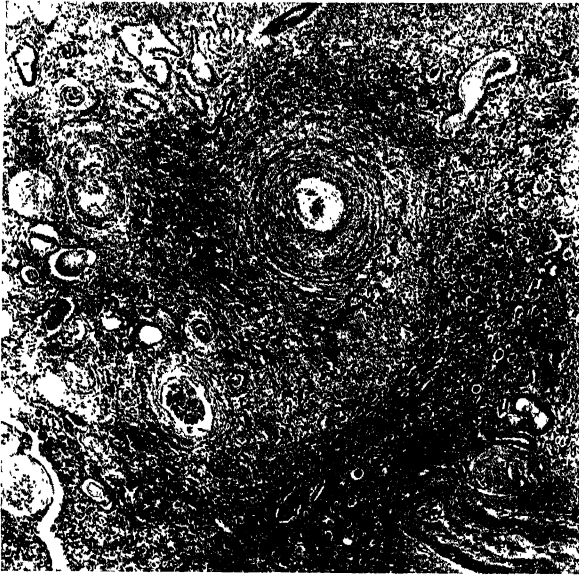
Fig. 404.—*Chronic Granular Contracted Kidney.* Shewing thickening of an interlobular artery, with atrophy and fibrosis of the neighbouring kidney-tissue, etc. (*see* text). ×50.

From obstruction to the blood-flow through groups of glomeruli, the corresponding interlobular artery is thrown out of use, and becomes thickened, and its lumen narrowed or even obliterated. This condition in the interlobular arteries may possibly, in some cases, be the primary one, the obliteration of the glomeruli being secondary to the cutting-off of their blood-supply, but probably the first-mentioned process is the more usual one. This slowly-produced obliteration of glomeruli and interlobular arteries has precisely the same effect as a similar blocking of a vessel from other causes, i. e. shrinking and atrophy of the area of distribution, and the penetration into the latter of small anastomosing vessels from the surrounding parts. In the case of the kidney, these vessels arise from the vessels of the capsule, and, by their penetration,

they bring about its adhesion at the parts of the surface corresponding to the distribution of the interlobular arteries. At these points also, depression of the surface, caused by the atrophy of the convoluted tubules, occurs. These new vessels give the characteristic red appearance to such a kidney, and, naturally, the redness will be most marked in the depressions or sulci on the surface; whilst the centres of the little "granular" areas may be pale, as these correspond to the tubules of the medullary rays or primitive cones described in the section on **Normal Structural Arrangement of the Kidney-Tissues,** p. 869.
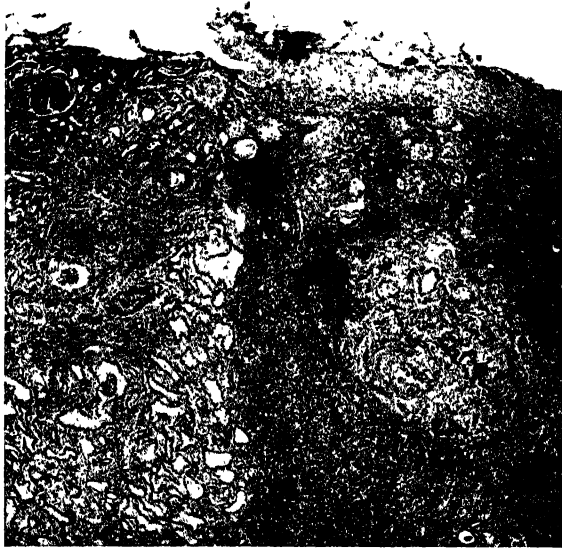
FIG. 405.—*Chronic Granular Contracted Kidney.* Vertical section towards surface, shewing (on the right) a dense fibrosed area corresponding to the obliterated inter-lobular artery and its glomeruli; and (on the left) an area with dilated tubules The thickened capsule has been removed from the surface of the latter area, but is still seen, *in situ,* at the upper part of the section, adhering to the dense area. × 50.

In these cases, there is not necessarily any great proliferation of **fibrous tissue** between the tubules, though this change is usually well marked around the obliterated glomeruli and inter-lobular vessels.

The **tubules** in the intervening areas, *i. e.* between the lines of the interlobular arteries, generally shew dilatation, catarrhal changes, casts, formation of cysts, etc.; and, therefore, on examining microscopically with a low power, the part of the kidney-section near the surface under the capsule, denser, irregularly wedge-shaped areas, with their bases towards the surface, will be found alternating with areas in which the tubules are irregularly dilated (*see* fig. 405). These denser areas often shew extensive overgrowth of connective tissue, containing obliterated glomeruli and atrophied and compressed tubules, though sometimes the

fibrous overgrowth may not be marked, especially in purely atrophic cases. The **Malpighian bodies** are very irregular in their distribution, being often huddled together in groups, owing to the atrophy of the intervening tubules. They shew all stages of the fibrous atrophy already described, varying from some which appear comparatively normal, to others which are entirely replaced by laminated fibrous scars.

ii. " **Large Pale Granular Contract**ing" **Kidney.**—In this condition, the size of the kidney varies greatly. The organ as a whole may be enlarged, or it may be normal or slightly diminished in size, and the term " large " is, therefore, a somewhat unfortunate one in this connection. Such
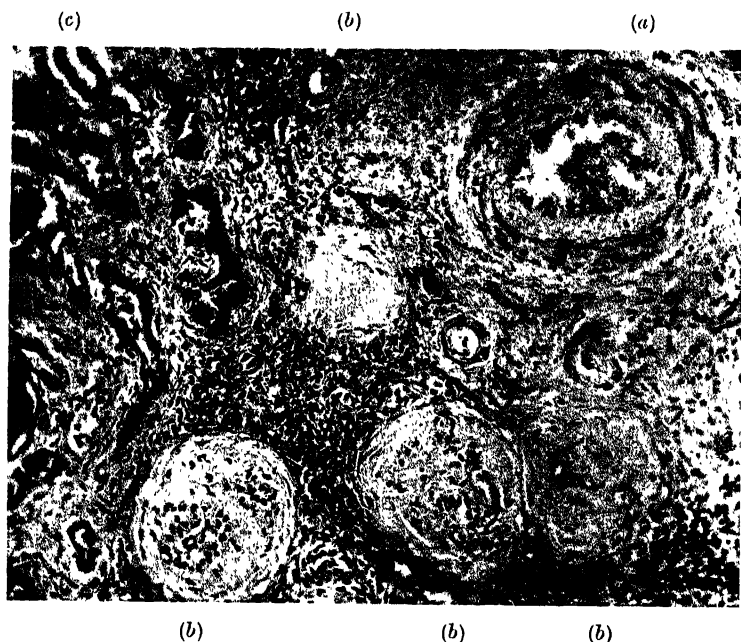
Fig. 406.—*Chronic Granular Contracted Kidney.* Shewing (*a*) partially obliterated inter-lobular artery; (*b, b*) groups of obliterated glomeruli corresponding to it; (*c*) altered tubules. × 130.

relative enlargement is due mostly to the swelling—which is sometimes very considerable—of the interpyramidal cortex, and this part of the kidney may shew considerable mottling from catarrhal and degenerative changes. Such a kidney is probably a more advanced stage of the subacute diffuse nephritis already described, where the condition is passing on to degeneration and atrophy. All intermediate forms are found, until finally the condition leads to the so-called—

iii. **Small Pale Granular Contracted Kidney,** in which large numbers of glomeruli, and, consequently, the corresponding interlobular, and perhaps even larger, vessels, have become obliterated. The condition is, therefore, one of **vascular obstruction,** and resembles the case of the purely atrophic or arterio-sclerotic kidney, except for the fact that it occurs

in a previously subacutely diseased organ, and hence some of the lesions found will owe their presence to this fact. Thus, if interstitial changes have been present, much more proliferation of fibrous tissue is found between the tubules than is seen in the purely atrophic forms.

The following are some of the conclusions of Gaskell,[1] which are, on the whole, very much in accordance with our own views. He divides the changes in the glomeruli and arteries of the kidney, which are not associated with pyogenetic or specific organisms, into two main groups : (1) **those accompanying and consecutive to acute inflammation of the kidney :** and (2) **those due to alterations which are primarily vascular in origin.**
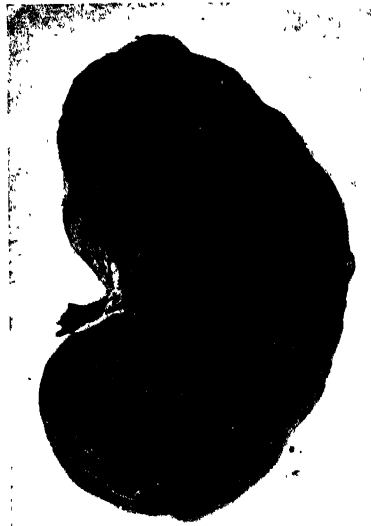
FIG. 407.—*Chronic Granular Contracted Kidney.* Shewing morocco-leather-like surface, from which the capsule has been stripped. A few small projecting retention-cysts are seen.

I. **The Inflammatory Group.**—There are two forms of " nephritis " in which the glomerular changes are negligible : one, primarily toxic, in which the convoluted tubules are mainly affected, e. g. in diphtheria and most other fevers, and in poisoning with corrosive sublimate and phosphorus : the other an acute interstitial nephritis, associated with the earlier stages of scarlet fever, characterised by great " round-celled infiltration " around the large vessels and, later, around the glomeruli—found only in cases which prove fatal in the first fourteen days of the disease, and thus, in this short period, not having established permanent functional change in the organ; whereas true scarlatinal " nephritis," which leads to permanent changes in the kidney, does not arise till the second, or more often the third, week of the fever.

Gaskell then proceeds to say, quoting Löhlein, that all forms of lasting nephritis are cases of **glomerulo-nephritis,** and that both the form usually

[1] J. F. Gaskell, " On the Changes in Glomeruli and Arteries in Inflammatory and Arterio-Sclerotic Kidney Disease." *Jour. Path. and Bact.*, Vol. XVI., No. 3, p. 287. January, 1912.

known as " large white " kidney, and the later " secondary contracted " kidney, always shew that they have arisen from an originally acute glomerulo-nephritis. At this point he carefully differentiates the embolic focal nephritis, due to multiple embolic infarctions from the heart-valves in cases of ulcera-tive endocarditis, from true glomerular nephritis. This has not been done by some writers, and has, accordingly, led to much confusion.

In his series of specimens of true **glomerulo-tubular nephritis,** only one case was examined in which death had occurred in the **early acute stage,** a fatal issue being rare at this stage. There is great **uniform swelling of the whole glomerulus,** and involvement of **all the glomeruli** --this diffuse character of the lesion being very important and characteristic. In the next, or **reparative, stage** of glomerulo-tubular nephritis, **all** the glomeruli are affected, with a variable amount of adhesion to their capsules. In the third, or **sclerotic, stage of secondary contraction,** death occurs commonly from **uræmia,** the urine shewing polyuria, much albumin, casts, and, at times, blood. The uræmic coma, preceding death, may be characterised by diminution, and finally by great diminution, in the quantity of the urine excreted. Blood-pressure is always high, 160 to 220 mm. of mercury in four of the cases in which this was recorded. The glomeruli shew further destructive changes.

In contrast with the foregoing, in **embolic focal nephritis,** the lesion is essentially hæmorrhagic in character, the urine is not greatly increased in quantity, and there is little albumin, the changes in the kidney affecting only **some** of the capillaries of **some** of the glomeruli. There is also marked fibrinous exudate, and great leucocytic infiltration. The tubules and inter-stitial tissue are not greatly altered, and there is, therefore, little naked-eye swelling. Gaskell believes that these changes are produced by the long-continued embolic loosening of infected material from the chief focus— subacute endocarditis—in the heart-valves, and he differentiates it, both clinically and anatomically, from the general glomerulo-tubular form previ-ously described.

II. **The Vascular Group.**- These fall into **two sub-groups**—

1. **The first,** due to the very slow alteration in the kidney produced **by senile arterio-sclerosis,** the age of the cases being usually over fifty years. The heart is seldom enlarged, and never to any great extent, unless valvular disease is also present. Practically all old people suffer from a greater or less degree of the condition. There may be some slight polyuria, and, at times, slight albuminuria. The aorta shews arterio-sclerosis, as does the main renal artery, the change spreading into the smaller arteries of the kidney in the regions where glomerular destruction and fibrosis are present. Only scattered glomeruli, or groups of glomeruli, are involved, the others remaining more or less normal in appearance. The affected glomeruli may be shrunken to half the normal size : their capsules thickened : and the capil-laries collapsed, but not otherwise altered; or the glomerulus may be com-pletely degenerated and fused to its capsule. The corresponding afferent arteries shew arterio-sclerosis, the longest vessels being earliest and most affected; whilst the shorter arteries and their corresponding glomeruli may still remain unaltered. There is little round-celled infiltration, a few cells, if present, being grouped round the atrophic tubules, corresponding to the affected glomeruli; the last stage in the degeneration of the latter being a mere fibrous-tissue scar. The contraction, therefore, supervenes especially along the most affected interlobular arteries, and the amount of the cirrhosis depends upon the relative degree of arterio-sclerotic change in these vessels, some being, in certain cases, often much more affected than others, and the change being, therefore, patchy in its distribution; or, if the interlobular

vessels are more or less diffusely affected, the cirrhosis is more uniformly distributed, and more finely granular in degree.

2. **In the second group** the changes are due to lesions which especially affect **the small arteries and arterioles, not only of the kidney itself, but of the various organs of the body.** They occur at an earlier age-period, especially between the ages of thirty and fifty years. The heart is always greatly hypertrophied, quite apart from any cardiac valvular lesion. These cases may be called genuine or **primary contracted kidney** (Adami), and should **not** be termed " small red," or " red contracted," kidney, as the senile arterio-sclerotic kidney may also be " red," and this term should be abandoned as misleading and obsolete. In this **primary contraction,** the change is essentially dependent on **alterations in the small arteries of the kidney.** This change in such small arteries **is not confined to the kidney,** but is also conspicuous in **other organs,** especially the **brain** and **spleen** the changes in the small arteries of the brain being of particular importance, and frequently leading to the occurrence of **cerebral hæmorrhage,** which is the direct cause of death in many cases of this class, such a termination being aided by the hypertrophy of the left ventricle and the high blood-pressure (over 200 mm.) practically always found. The aorta may shew a smooth inner wall, or only slight fatty change in the intima; and the renal artery presents a varying, but definite, arterio-sclerotic change. The arterial renal arches also shew some varying degree of this process; but the most conspicuous and important change is extreme thickening of the intima of the **smallest arteries of the kidney,** especially the **afferent and also the interlobular arteries.** The lumen may be extremely narrowed, and the enormously thickened vessel-wall often contains a large amount of fat. Elastic tissue is also highly developed in all the renal arteries, both large and small. The thickening of the vessels is very much greater than in the senile arterio-sclerotic form.

Gaskell further subdivides these primary contracted kidneys into various groups, but, for the detailed description of these, reference should be made to his original paper.

NOTE ON TRENCH NEPHRITIS. —In the late war, and also in the American Civil War, during the prolonged periods of trench fighting, large numbers of cases of acute nephritis occurred. After eliminating the various forms of acute and chronic nephritis equally typical of civil life, a large proportion of cases remains, characterised by **dropsy** (which usually rapidly subsides), **diminution** or even **temporary suppression of the urinary secretion,** marked **albuminuria,** often persisting for a considerable time, **hæmaturia,** the presence of **renal casts,** especially of granular and hyaline type, **uræmic symptoms,** etc. In comparison with the severity of the clinical symptoms, the mortality is extraordinarily low, only three deaths occurring in 1,455 cases reported by Rose Bradford,[1] and these three cases not showing a picture of uncomplicated nephritis. No authoritative work on the actual causation of the disease has yet appeared, but as far as our present knowledge goes, the pathological lesion in the kidney itself is a **subacute diffuse nephritis,** glomeruli and tubules being both specially affected.

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[1] *Quarterly Journal of Medicine,* January 1916, p. 125.

Note.—Short Résumé of some of the Naked-Eye Changes in the Kidney seen in various cases of Bright's Disease, with their causes :—

1. **Thickening and Adhesion of the Capsule**—due to establishment of a supplementary circulation from branches of the lumbar arteries, and **not** to inflammatory changes such as cause thickening and adhesion, say, of the two layers of the pleura.

2. **Cysts**—formed by blocking and dilatation of tubules, or, much more rarely, of the glomerular capsules. Tubules may be blocked by :—(i) Colloid or other forms of casts : (ii) compression from chronic fibrous overgrowth and contraction, and therefore specially found in chronic granular contracting kidneys, and also in larger forms of waxy kidney with interstitial changes,

3. **Swelling of the Cortex** —may be due to :—(i) Hyperæmia and distension of the vessels : (ii) cloudy swelling, etc., of epithelium : (iii) glomerular changes, e. g. hyaline or other forms of swelling of the capillaries of the tuft : also of its connective tissue and covering epithelium : leucocyte-emigration : swelling of Bowman's capsule or of its lining endothelium, etc. : and to (iv) interstitial changes.

4. **Contraction of the Cortex** - may be due to atrophic changes, especially those resulting from vascular and glomerular lesions : and, to a less extent, to contraction of fibrous tissue or to senile changes.

5. **Pallor of the Cortex** -may result from :—(i) Cloudy swelling and catarrh : (ii) interstitial overgrowth : or from (iii) fatty and necrotic changes.

6. **Mottling of the Cortex** —may occur from marked fatty degeneration, or from catarrhal and necrotic changes. It is seen in its most exaggerated form where these changes are intermingled.

7. **Irregular Striation of the Cortex** or " distortion of the vascular markings " in granular contracted kidney, is due to slow atrophic changes.

8. **Vascular Engorgement** - generally venous in character - specially affects (i) the stellate veins on the surface, and sometimes also the capillaries ; (ii) the venæ rectæ, forming red striæ in the pyramids, especially towards their bases ; (iii) the interlobular veins, glomeruli, and intertubular capillary plexus in the cortex ; and (iv) the vessels of the pelvis, especially those of its submucous coat.

9. **Thickening of the Arteries** - may be part of a general condition throughout the whole of the vascular system, and is often especially marked in the kidney. In other instances, it may be due to local disease in the kidney itself, especially to obliteration of the glomeruli.

10. **Increase of Fat around the Renal Pelvis** --is found in atrophic conditions where the kidney-tissue shrinks, and consequently the hilus is enlarged.

Note on Albuminuria.—In renal cases, albuminuria may be found in any disease damaging the organ and causing transudation of serum or hæmorrhages into the tubules or glomeruli. But some cases of even advanced chronic renal disease may go on to a fatal issue with no, or with only occasional, albuminuria—the excretion of water being, however, usually increased, and the urea diminished.

HYDRONEPHROSIS.—This is a condition of dilatation of the pelvis of the kidney and its calyces. It may arise from any cause which impedes the outflow of urine from the renal pelvis, and is greatest in those cases where the obstruction is either incomplete or intermittent. When the outflow of urine from the pelvis is completely and permanently stopped, a certain degree of dilatation takes place ; but the increased pressure prevents further secretion of urine by the kidney, which, as a result of loss of its function, undergoes atrophy. In such a case, the accumulated fluid may

undergo, more or less complete absorption; and shrinking of the kidney, with associated fibrous-tissue overgrowth, may result. Where the obstruction is incomplete, the kidney, although its glandular structure becomes distended, is still able to carry on its functions and supply fluid for the further gradual distension of the pelvis. When this dilatation becomes excessive, atrophy of the kidney-tissue may supervene, often, however, not until the hydronephrotic organ has reached a very considerable size (see fig. 408).

Fig. 408.—*Hydronephrosis of Kidney due to obstruction of the Ureter.* The renal pelvis and infundibula or calyces are enormously dilated, and the glandular tissue is completely atrophied. (Edinburgh University Anatomical Museum. Catalogue No., Gen.-U. B. c. 9.)

The commonest **causes** of hydronephrosis are stricture of the urethra or ureter; certain malformations of the latter, more especially the presence of abnormal kinks or bends (see fig. 388, p. 866); the impaction of a calculus in the ureter or urethra; or the occurrence, in these structures, of chronic inflammatory changes or tumour-growth, the latter acting either by pressure or by actual infiltration of the walls. Another, and fortunately much rarer, cause, but one of which several cases have been recorded, is injury, or even accidental ligature, during operation, e.g. for the removal of pelvic tumours. •Where the obstruction is in the urethra, or where

it involves the openings of both ureters into the bladder, as, for example, by tumour-growth, the condition is **bilateral,** though not necessarily symmetrical, on the two sides. In such cases, the **ureters** also are dilated, sometimes to a remarkable degree. Frequently, this distension of the ureters is not uniform, but is characterised by the formation of irregular saccular dilatations. In some instances, the condition may be **congenital,** as, for example, in cases of extreme phimosis, or where the urethra is impermeable at birth, or where there are abnormal kinks or valvular bends upon the ureters. On the other hand, in some of these congenital cases of hydronephrosis, no obvious cause of obstruction to the outflow of urine is demonstrable. **Unilateral** hydronephrosis results from the implication of one ureter by stricture, impacted calculus, or other lesion, the ureter above the seat of obstruction also undergoing dilatation.

Fig. 409.—*Coralline Calculus* occupying Pelvis and Calyces of Kidney, the glandular tissue of which is greatly atrophied. The central limb of the calculus has been broken off to show the bed in which it lay. (Edinburgh University Anatomical Museum. Catalogue No., Gen.-U. B. g. 2.)

Results.—Catarrhal pyelitis and **secondary changes in the kidney,** somewhat resembling those seen in chronic granular contraction with interstitial overgrowth, are usually found, but complete **fibrous atrophy,** with entire disappearance of all the glandular tissue, may occur (*see* fig. 408). **Suppuration** may take place, the condition then becoming one of **Pyonephrosis** (*q. v.,* p. 887).

RENAL CALCULI AND CONCRETIONS (NEPHROLITHIASIS). Calculi may be formed in the pelvis of the kidney or in any of its diverticula or calyces; or, again, they may originate in the renal tubules, more especially in the larger collecting tubules near their openings at the apices of the papillæ. Renal calculi may be carried downwards and become impacted in the ureter, leading to hydronephrosis; or, if small enough, they may reach the bladder, their passage down the ureter giving rise to an attack of "**renal colic.**" In the bladder, they may act

as the nuclei around which further concretions are formed; or, if not too large, they may pass through the urethra and be found in the urine as the so-called urinary " gravel." In some instances, they may, partially, or almost completely, fill the pelvis of the kidney and its calyces, forming the so-called **coralline calculus,** which may either be single (*see* fig. 409), or composed of two or more faceted constituent parts. In some instances, several, or even very many, small calculi may be found in the pelvis, in its calyces, or in the renal substance. **Both** kidneys may be the seat of calculus-formation, especially in the later stages of the disease, and are, therefore, more frequently found to be so affected on *post-mortem* examination (about fifty per cent. of cases) than in surgical practice.

Composition of Renal Calculi.—Such calculi may consist of **uric acid, urates, phosphates, oxalates,** or **carbonates,** or varying **admixtures** of these substances. More rarely, they may be composed of **cystin, xanthin, bile-pigment** (in long-standing jaundice), etc. Calculi are commonest in mid-adult life, but may occur very early in life, the phosphatic being the commonest form found in childhood.

Ætiology and Results.—The causes of urinary calculus-formation in general will be discussed when dealing with calculi formed in the urinary bladder (*see* p. 924). In the case of the kidney, various lesions may be present, either aiding in the production of, or consecutive to, calculus-formation, or both may have some factor common to their causation. Thus, the condition may be found along with various forms of **nephritis, diffuse,** or especially **interstitial, chronic granular contraction,** partial or complete **atrophy** of the kidney, **perinephritis,** etc. Infective lesions are common. There is often an associated **pyelitis** and **pyelonephritis,** which may, perhaps, have some causal relationship; whilst, on the other hand, the presence of calculi may lead to such conditions, or further aggravate them if already present. In addition to such inflammatory phenomena, renal calculi may cause **hæmorrhage,** and also, as already mentioned, may become impacted in the ureter, and give rise to **hydronephrosis** or to **pyonephrosis,** and to **renal colic.** If carried down into the bladder, they may, as already indicated, constitute the nuclei for further calculus-formation in that organ.

Sometimes the substances of which calculi are composed—especially uric acid, urates, or lime-salts —may be deposited, in crystalline or in amorphous form, **in the renal tubules,** especially in the pyramids towards their apices. A deposit of lime-salts may occur in necrotic renal epithelium, *e. g.* following poisoning by corrosive sublimate, etc.; and, similarly, " incrustation " with calcareous material may occur in the walls of the renal pelvis and ureter, the process being also probably secondary to degenerative and necrotic changes in these structures.[1] In the same way, bile-pigment may be deposited in a similar position *e. g.* in icterus neonatorum, and in chronic jaundice in adults.

(For a further description of **Urinary Calculi** *see* p. 924.)

[1] Caulk, *Journal of Surgery, Gynæcology and Obstetrics*, 1914, i., p. 497.

CIRCULATORY DISORDERS OF THE KIDNEY :—

(a) **ACTIVE HYPERÆMIA OF THE KIDNEY** may be found in cases of convulsions, for example in **epilepsy ;** and, in such cases, a, **transitory albuminuria** and **hæmaturia** may occur. A similar condition has been described in **traumatic lesions of the vaso-motor centre in the medulla.** More commonly, however, it occurs in the **acute infective fevers,** and after the administration of such **poisons** as cantharides, corrosive sublimate, arsenic, carbolic acid, etc., and may then be regarded as either preliminary to, or as part of, an acute inflammatory attack.

(b) **PASSIVE** or **VENOUS CONGESTION** may be **acute** or **chronic,** the latter especially being a very common condition.

Fig. 410.—Acute Congestion of the Straight Vessels towards base
of Malpighian Pyramid. × 75.

Acute Venous Congestion may occur with great rapidity, for example in **opium-poisoning,** and in some cases of coma from other causes. In its most intense form, it is found as a sequel to **obstruction of the renal vein** from thrombosis, ligature, torsion of the vessels in a floating kidney, or other cause. The changes occurring in the organ are fully described on p. 122. Thrombosis of the renal vein may be produced by direct extension into it of a thrombus of the inferior vena cava, by the pressure of a tumour on the vein, or by similar causes. If the renal artery remains patent, intense congestion occurs, usually accompanied by hæmorrhages into the glomeruli, the tubules, and perhaps also into the pelvis of the kidney.

Chronic Venous Congestion of the Kidney is an extremely common

condition, due, in the majority of cases, to **old-standing heart-disease,** especially to lesions of the mitral valve, the. condition being sometimes termed "**cardiac kidney.**" Chronic venous congestion may also, but much more rarely, be produced by **local interference with the venous return,** as, for example, by the pressure of a tumour upon the renal vein or on the inferior vena cava, or from mechanical displacements of the organ, as in floating kidney.

The **naked-eye appearances** of the kidney may vary considerably if other lesions are associated with the chronic venous congestion. In an uncomplicated case, the organ is usually moderately enlarged. Its capsule may be slightly thickened and somewhat adherent, and the
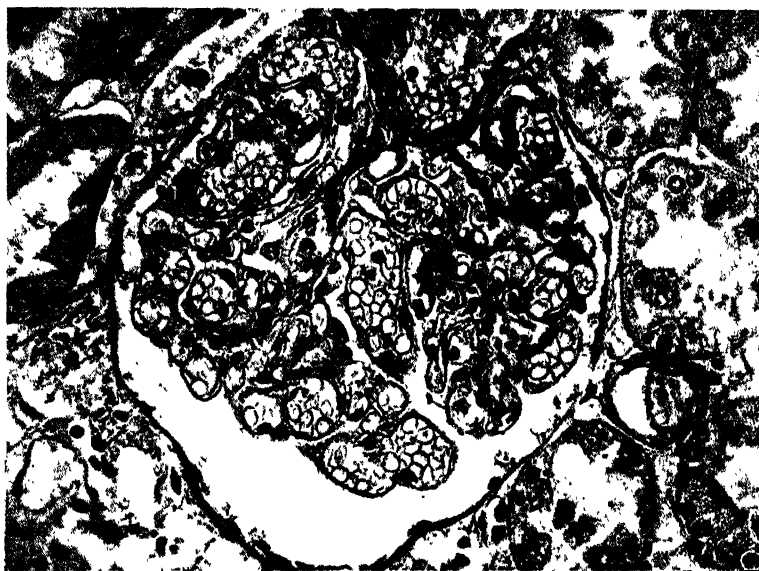
Fig. 411.—Acute Congestion of Glomerular Capillaries. × 300.

cortex usually shews, at first, some increase in volume; but, at a later period, a certain degree of atrophy, especially in its inter-pyramidal portions, takes place. This atrophy is due to interference with the nutrition and functions of the tubules, and may lead to the production of a slightly granular or morocco-leather-like surface. **On section,** the larger veins are dilated, whilst the engorgement of both sets of tributaries of the venous renal arches maps out the minute naked-eye structure of the organ very distinctly. The venulæ rectæ stand out prominently as dark-red radiating lines, which are usually most marked towards the bases of the pyramids; whilst, in the cortex, the alternation of the pale medullary rays with the engorged lines of the inter-lobular vessels can be very definitely seen. If the dark lines corresponding to the engorged inter-lobular veins be closely examined, the glomeruli can usually be seen as

minute, dark-red dots, giving a finely-stippled appearance to the vascular markings. The stellate veins on the surface are congested, and the organ is distinctly firmer in consistence and darker in colour than when normal.

On microscopical examination, the pathological appearances are usually best seen at the bases of the pyramids in the bundles of straight venules, the walls of these being thickened and their lumina distended with blood. The Malpighian tufts are enlarged, the capillaries being

Fig. 412.—*Kidney.* Venulæ Rectæ towards base of Pyramid in Chronic Venous Congestion. × 60.

dilated and their walls thickened. Similar dilatation and thickening are seen in the interlobular veins and intertubular capillary plexus. The increased firmness of the kidney is due to this engorgement of the veins and capillaries and to the thickening of their walls, and not to proliferation of the connective-tissue framework of the organ. Some degree of atrophy may supervene in the tubular epithelium, and catarrhal changes, especially in the collecting tubules, may be present. In uncomplicated cases, however, such structural changes are not specially marked. Minute hæmorrhages from the glomerular tufts sometimes occur, and the blood may, in severe and advanced cases, find its way even into the tubules, and be passed into the urine. As a rule, however, hæmaturia, in such
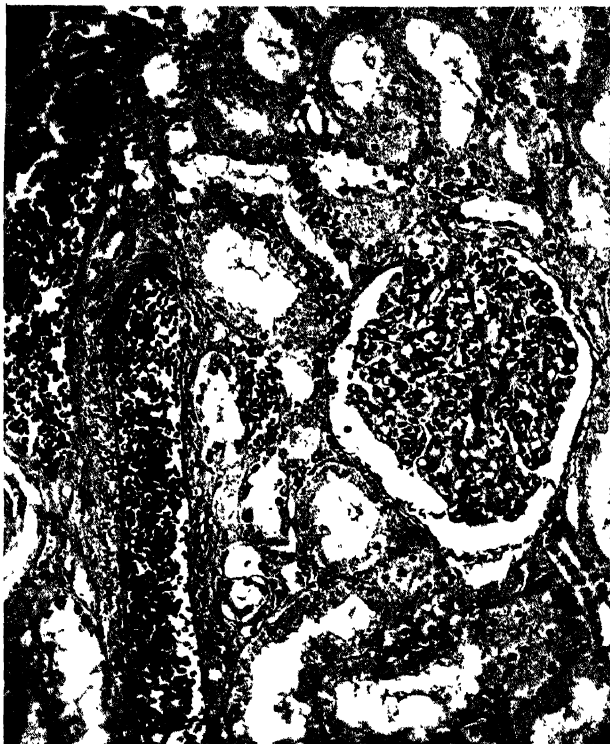
Fig. 413.—*Kidney*. Shewing Chronic Venous Congestion of Interlobular, Intertubular, and Glomerular vessels. × 160.
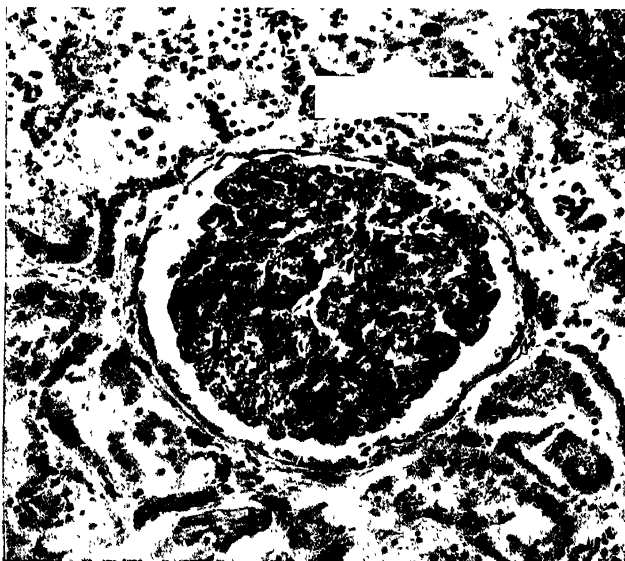
Fig. 414.—*Kidney*. Glomerulus shewing Chronic Venous Congestion. The Intertubular Capillaries also shew engorgement. × 160.

cases, indicates the presence of some complication, especially the occurrence of embolism and infarction, conditions not infrequently associated with chronic venous congestion arising from mitral disease.

(c) **EMBOLISM and INFARCTION.**—These conditions, and the characteristic lesions produced by them, are fully described on pp. 144–160. **Infarcts** of various sizes and at various stages—from those newly formed to those which have become completely absorbed and shew merely as puckered and depressed fibrous-tissue scars—may occur in the kidney.

The occurrence of **Septic Embolism** and **abscess-formation** in ulcerative endocarditis and in pyæmia from other causes, is discussed under **Suppurative Nephritis** on p. 884.

(d) **HÆMORRHAGES** into and from the kidney—apart from traumatic causes such as rupture or penetrating wounds –frequently occur in intense **toxic poisoning,** especially when this is characterised by acute venous engorgement. Such extravasations of blood are usually comparatively slight. They are found especially in or around the glomeruli and in the tubules. Hæmorrhages into the interstitial tissue are comparatively rare. They may originate from the subcapsular vessels, and from the straight vessels in the boundary zone. More severe hæmorrhages, especially from the mucous membrane of the pelvis, tend to occur in **purpura, scurvy, leuco-cythæmia,** and other blood-diseases. Bleeding may also take place as a result of the presence of **tumours** and **calculi.** Minute submucous petechial hæmorrhages are of common occurrence in many acute toxic and septicæmic diseases; and an **intense hæmorrhagic nephritis** may, in certain cases, supervene in some of the acute infective fevers, e. g. epidemic cerebro-spinal meningitis.

SPECIFIC OR CHRONIC INFECTIVE DISEASES OF THE KIDNEY :—

(a) **TUBERCULOSIS OF THE KIDNEY.**—This may be part of a general acute or chronic tuberculosis, but, in some cases, the disease is more or less limited to the genito-urinary system.

In **General Acute Miliary Tuberculosis,** the tuberculous granulations are of common occurrence in the kidney, especially in the cortex, where they may extend along the lines of the interlobular vessels. In a considerable proportion of cases in which they are few in number, they may be found on the surface immediately beneath the capsule. In other cases they may be numerous both on the surface and throughout the section. They shew as minute, rounded, opaque white areas, similar to those seen in the other organs; or they may appear as elongated masses in the long axis of the vessels, produced either by extension or by the coalescing of adjacent nodules. Towards the surface, they may be somewhat wedge-shaped. It is occasionally a matter of difficulty to distinguish them, with the naked eye, from small abscesses, but, under

the microscope, they exhibit the usual appearances of caseation, and the other changes characteristic of tuberculous lesions elsewhere.

Fig. 415.—*Infarcts in the Kidney.* Shewing raised wedge-shaped area, with pale centre and congested hæmorrhagic periphery.
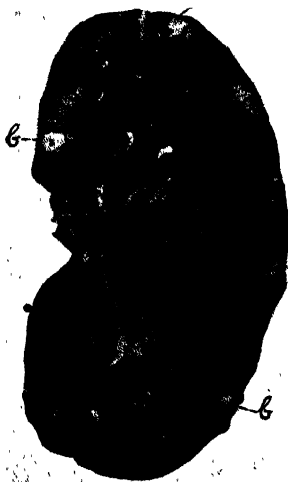
Fig. 416.—*Infarcts in the Kidney.* Shewing the pale centre and congested periphery. Note that the surface level of the Infarcts is slightly depressed below the general surface of the Kidney. *a,* Infarct extending into medulla. *b, b,* Smaller Infarcts confined to cortex.

In cases of chronic tuberculosis in other organs, a few small, widely-scattered tubercles in the kidney are of comparatively common occurrence; whilst, in children especially, somewhat larger caseating areas may be found in this organ.

60

Genito-Urinary Tuberculosis or **Renal Phthisis** is the most important form in which the disease attacks the kidney. This condition is often, though by no means invariably, associated with the presence of tuberculous lesions elsewhere, for example in the lungs, pleuræ, etc. It is commonest in the male, and frequently is first recognised clinically in the **globus major of the epididymis,** from which it may come to involve the **body of the testicle** and the **vas deferens.** By way of the latter—usually along its lymphatics—the process spreads to the **seminal vesicles, urethra** and **bladder,** and up the **ureters** to the **pelvis of the kidney.** In other cases, again, the disease may—either from hæmatogenous or lymphatic infection, or by spread from a focus within the kidney—affect the submucous coat of one of the renal pelves, from which position it spreads downwards, involving the ureter, bladder, etc. It may then extend upwards along the other ureter, and attack the kidney of the opposite side. Thomson Walker[1] states that, " clinically, tuberculosis of the kidney is very frequently found without vesical tuberculosis, and the after-history of cases of nephrectomy shews that the original focus was in one kidney." He is of opinion that " of the three paths of infection (ascending, hæmatogenous, and lymphatic) there is more evidence in favour of the hæmatogenous than of the others. By whichever method the disease reaches the pelvis of the kidney, it speedily attacks the mucous membrane, especially in the calyces immediately around the renal papillæ, where caseous ulcers are formed, external to which there is a zone of intense congestion. These gradually spread into the substance of the kidney, which may become converted either into a caseous mass or— if the ureter is partially or wholly obstructed by the tuberculous process— into a series of sacs and pouches with caseous walls and contents, these corresponding to the dilated and ulcerated calyces. The size of such a kidney varies with the degree of obstruction and the amount of distension produced, the organ being, in some instances, very greatly enlarged. This enlargement, however, is not a constant feature—the kidney being sometimes normal, or even reduced, in size. In the substance of the kidney, beyond the line of ulceration, groups of tubercles may be found, but in some cases these are absent. There is usually an attempt to shut off the diseased area by the formation of a zone of fibrous tissue, as in tuberculous lesions elsewhere. **Associated lesions** in the kidney-tissue, such as acute nephritis, subacute diffuse and interstitial nephritis, waxy disease, etc., may be present. Fibrous changes in the capsule and surrounding fatty tissue, with adhesions to neighbouring structures, are practically always found.

As a rule, in *post-mortem* cases, **both** kidneys are affected, though frequently in varying degree. In *ante-mortem* cases coming under the observation of the surgeon, Thomson Walker states that from 88 to 92 per cent. are unilateral, though it is obviously extremely difficult; if not impossible, to be absolutely certain in the living subject, that the other

[1] Thomson Walker, *loc. cit.*, p. 227.

organ is entirely unaffected. He considers that spread to the opposite
kidney is usually by way of the blood-stream. In cases where one kidney
only is diseased, the right organ is more frequently affected than the left.
In cases in which the disease commences on one side, and extends to the
bladder and up the opposite ureter, both **ureters** become swollen, thickened,

Fɪɢ. 417.—*Tuberculosis of Kidney*—" Renal Phthisis." The kidney-substance has been
almost entirely replaced by large cyst-like cavities, which have resulted from the
progressive ulceration and dilatation of the pelvis and its calyces. The walls of these
spaces are ragged and caseous. (Edinburgh University Anatomical Museum. Cata-
logue No., Gen.-U. A. q. 3.)

and hard, and more or less filled with caseating material, this causing a
diminution in calibre or even entire obliteration of the lumen. In the
bladder, the infection may lead to cystitis, catarrhal changes, and perhaps
to extensive ulceration; though, in some cases, the tuberculous lesions
are localised especially to the region of the **trigone.** In the **epididymis,**
as already mentioned, the tuberculous process, in addition to involving
the **vas deferens,** may spread to the testis, usually, at all events at first,
on one side only. The vesiculæ seminales may also become involved.

Results.—Most commonly, genito-urinary tuberculosis is a steadily progressive disease leading to a fatal termination. In a few instances, however, the process may be arrested, the caseous material becoming inspissated and perhaps calcified, and surrounded by dense fibrous tissue corresponding with the capsule of the organ. Such instances of " healed " tuberculosis of the kidney may sometimes be found in the bodies of even very old persons, in whom the presence of genito-urinary tuberculosis. had been quite unsuspected during life.

(b) **ACTINOMYCOSIS.**—This may affect the kidney as part of a generalised spread from some focus of disease in connection with. the intestine, appendix, or elsewhere, or the condition may spread to the organ by direct continuity. In the former case, multiple small nodules, tending to soften and form small abscesses are found. A perinephritic abscess may supervene. The condition is rare.

(c) **SYPHILIS.**—The effects of **syphilitic disease** upon the kidney are often profound. **Gummata,** and the irregular contracting **fibrous cicatrices** resulting from them, may occur; the vascular lesions, especially in the renal arteries, are very important; but the most characteristic lesions produced in the kidney by syphilis are **waxy** and **interstitial changes.**

Waxy or amyloid degeneration is one of the commonest evidences of the disease, and is often associated with interstitial changes, and the formation of cysts. In such syphilitic waxy kidneys, the capsule is not necessarily thickened or unduly adherent, and the surface of the organ is usually granular, the elevations being larger and more irregular than those seen in granular contracted kidney. The uneven surface frequently presents an undulating character. Unless other causes are also present, these changes in the kidney are not necessarily—and, in fact, are seldom— accompanied by hypertrophy of the left ventricle. (For a more detailed account of **waxy or amyloid** disease of the kidney, see pp. 62 and 873–4.)

(d) In **LEUCOCYTHÆMIA,** especially in the "**lymphatic**" forms, characteristic changes are found in the kidney. The interstitial connective-tissue framework of the organ, especially around the vessels, is infiltrated with cells of the leucocyte-series, the nature of which varies with the type of the disease—the smaller or larger lymphocyte-like cells being present in the lymphatic, and myelocytes and immature polymorphonuclear cells in the myelogenous, variety (see pp. 611 and 609).

TUMOURS OF THE KIDNEY :—

To the formation of **Cysts** of various kinds, reference has already been made on p. 865 (see also p. 344).

Simple Tumours.—If the common small "fibromas" be excepted— simple tumours constitute less than seven per cent. of renal growths. **Fibromas**—or little fibrous nodules indistinguishable histologically from these—are of extremely common occurrence in the kidney, more especi-

ally in the pyramids, where they are seen, on section, as small, firm, white nodules, usually about the size of a hemp-seed or a little larger. They are believed by some to be of the nature of hamartomas or " deficiency-tumours " (see p. 287). **Lipomas** may occur in, but more commonly around, the kidney. Multiple small lipomas are sometimes found immediately under the capsule.

Sarcomas, especially **round-** and **spindle-celled** in type, may occur, as may also **lymphomatous** and **lympho-sarcomatous tumours**—the last-mentioned most commonly in infancy and early childhood. Such sarcomas, when thus occurring in infants, are sometimes of enormous size; and, if present in the fœtus, they may interfere with parturition. In the adult, such tumours are usually relatively smaller—rarely larger than an infant's head. They are generally spindle-celled or small round-celled in type. **Rhabdomyomas** and **Myosarcomas,** or congenital tumours containing peculiar aberrant forms of striped muscle, often mixed with connective tissue of primitive or sarcomatous type, are extremely rare forms of malignant growths in the kidney. They are found usually in early infancy, and are regarded as due to the embryonic intermingling of tissues. The occurrence of such tumours in the kidney may be one of the peculiar associated phenomena characteristic of **tuberose sclerosis** (q. v., p. 998, and also pp. 299–301 and 532). **Leiomyomas** are very rare. They have been described as occurring on the surface under the capsule.

Simple Adenomas originating in kidney-tissue proper are of extreme rarity, but adenomatous tumours, arising from **suprarenal remnants** or " **rests,**" and to which allusion is made in the Chapter on **Tumours** (p. 271 ; see also p. 854), are of more frequent occurrence. Aberrant or displaced portions, or even the whole, of the suprarenal body, may be found partially or entirely embedded in the renal cortex, from which they are usually demarcated by a distinct fibrous-tissue capsule. They are seen commonly as small, more or less regularly rounded masses, immediately under the capsule, projecting slightly above the general surface, and presenting the finely-mottled, orange-yellow or yellow-ochre colour characteristic of the suprarenal cortex itself. From these rests—which, as a rule, shew almost the normal microscopical characters of the cortex of the suprarenal gland itself—tumours, both simple and malignant, may arise. Such tumours—**Hypernephromas,** as they have been termed—are most commonly found in patients over fifty years of age. They are situated usually towards the upper end of the kidney, and may vary in size from that of a walnut up to that of the closed fist, or even larger. They are, as a general rule, irregularly rounded, and sometimes nodulated, and grow inwards towards the pelvis, the kidney-tissue becoming compressed and atrophied—a distinct line of demarcation usually being seen between the two. On cutting into the tumour, the section may present a peculiar nodular and variegated appearance, due to the intermingling of orange-yellow suprarenal-like tissue, with areas of hæmorrhage, and of

degeneration and necrosis—which are of comparatively common occurrence. Occasionally, also non-striped muscle-fibres, areas of cartilage, and even of bone, are found, such tumours being apparently either of the nature of embryomas, or due to the intermingling of tissues early in development. These complex tumours vary greatly in their degree of malignancy. They may be comparatively simple and slow-growing,

FIG. 418.—*Mixed Malignant Tumour of Kidney*, originating, perhaps, as an embryoma, or possibly from the inclusion or intermingling of neighbouring tissues during embryonic life. The tumour contains areas of imperfectly-formed cartilage, small cystic adenomatous spaces, and masses of aberrant suprarenal tissue. The dark areas are due to extensive haemorrhages into the tumour. (Edinburgh University Anatomical Museum. Catalogue No., Gen.- U. A. w. viii. 3.)

with little tendency to infiltrate neighbouring organs and tissues, and they may not give rise to metastases; but, in other cases, they are more actively malignant, increasing rapidly, and producing secondary growths in the liver, lungs, bones, etc., and also, not infrequently, in the other kidney.

Primary Cancers of the kidney are comparatively rare and may be of malignant adenomatous type. They may be primary in, and limited to, one kidney; but it is common, in these cases, to find

secondary growths in the opposite kidney. Such tumours may be characterised by the presence of numerous cystic spaces, due to the blocking and dilatation of kidney-tubules. Encephaloid or soft cancers, sometimes containing very large cells, occur; and, in some cancerous tumours, ciliated epithelial cells have been found.

Secondary growths arising from tumours elsewhere are not specially common in the kidney, but, when they do occur, they may be very numerous. Both cancers and sarcomas are found, especially melanotic forms of the latter.

Hæmaturia is present in the majority of cases of malignant disease of the kidney, but is liable to occur especially in **malignant papilloma** of the mucous membrane of the **pelvis**. With this type of tumour, calculi are found associated in about 50 per cent. of the cases.

PARASITES IN THE KIDNEY :- - *

Hydatid Cysts are rare. They may either be confined to this organ, or accompany a similar condition of the liver.

Schistosomiasis (Bilharziasis) may attack the mucous membrane of the pelvis.

Eustrongylus Gigas, a very rare parasite in man, has been described as occurring, coiled up within the pelvis of the organ.

DISEASES OF THE URINARY BLADDER

CONGENITAL ABNORMALITIES.--Malformations.—The main portion of the bladder is formed developmentally from the upper part of the anterior division of the entodermal cloaca; whilst the smaller basal portion, roughly corresponding to the trigone, arises from the opened-out lower ends of the Wolffian ducts, and is, therefore, of mesodermic origin. The upper or cephalic end of the bladder narrows gradually, and is continuous with the proximal part of the allantois, which should normally close about the fifth week of intra-uterine life (Dixon).[1] Owing to the incomplete closure of these structures anteriorly, varying degrees of malformation, from **umbilical fistula** up to complete **extroversion of the bladder,** may occur. In the latter condition, the anterior wall of the abdomen between the pubes and the umbilicus, and the front wall of the bladder, are deficient. The cleft so formed is lined by the posterior wall of the organ, the margins of which are continuous with the skin of the abdomen. In consequence of the intra-abdominal pressure acting upon the soft, yielding bladder-wall, it is protruded through the incomplete abdominal parietes, forming an irregular, bulging mass, varying in size, and covered by congested,

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[1] Dixon, in Cunningham's *Textbook of Anatomy*, Henry Frowde and Hodder & Stoughton, Edinburgh, Glasgow and London, 4th edition, 3rd impression, revised, 1917, p. 1332.

and—from its exposure to bacterial infection—usually inflamed, mucous membrane, on which the openings of the ureters can be seen, inter-mittently discharging urine during life. With this bladder-condition, there are usually associated **malformations of the urethra and external genitals,** more especially **epispadias** or incomplete closure of the urethra along the dorsal aspect of the penis, which itself usually remains small and rudimentary. The pubic arch may be incomplete towards the middle line.

Minor degrees of non-closure are also found, either at the upper, or at the lower, end of the original cleft. The **urachus** or intra-abdominal portion of the allantoic canal **may remain patent,** producing a urinary fistula, running from the apex of the bladder up to the umbilicus, where it opens on to the surface. In other instances, only certain portions of this canal persist unclosed, and may, by their subsequent distension, give rise to **cystic formations.** From defective closure at the lower end, varying degrees of **epispadias** are produced (*see* p. 926).

INJURIES.—**Rupture** of the bladder, with **extravasation of urine** into the peritoneal cavity or into the cellular tissue, etc., may occur, especially in crushing injuries causing fracture of the pelvis. Injury to the bladder may be produced by penetrating wounds, or during parturition; and also in cases of falls from a height, or blows on the abdomen when the bladder is distended with urine. For a detailed account of these and other conditions, reference should be made to textbooks on Surgery, Midwifery, and Gynæcology.

DILATATION of the bladder, with or without **HYPERTROPHY** of its muscular walls, is of comparatively common occurrence. **Acute distension** may be due to obstruction of the outflow of urine, *e. g.* from congestion of the prostate, especially where the so-called middle lobe of the gland is enlarged. Such acute distension may also be due to paralysis of the muscular coat of the organ, and may be very great in degree.

Where the dilatation is **gradually** produced, *e. g.* in cases of urethral stricture, a very considerable degree of **hypertrophy** may occur, more or less uniform in some cases, but in others extremely asymmetrical, the thick, interlacing bundles of muscle, when viewed from within, often resembling the pectinate muscles of the heart. Between these bundles, **pouch-like dilatations** or **diverticula,** sometimes of considerable size, may be produced—a condition known as **sacculation of the bladder.** Where once formed, such diverticula tend to become progressively larger in size. In these sacculi, **calculi** may form, deposits of triple phosphates being common, especially if any infection, leading to decomposition of the urine, occurs. Diverticula may also, in some cases, be **congenital** in origin, *e. g.* those arising from a persistent urachus (*see above*).

HÆMORRHAGE INTO OR FROM THE BLADDER.—Apart from conditions in which the blood reaches the bladder **from above,** *e. g.* from the kidney or renal pelvis, hæmorrhage may occur in cases of trauma

(accidental or operative), in **calculus-formation,** in **blood-diseases** (*e. g.* hæmophilia, scorbutus, etc.), in some cases of **poisoning** (*e. g.* with canth-arides), in certain very **acute forms of cystitis,** and in cases of **tuberculous ulceration, new growth,** and **schistosomiasis (Bilharziasis** or **endemic hæmaturia).** Bleeding from the bladder-wall may also be produced **if the urine from an over-distended bladder be too quickly drawn off.** This is due probably to the sudden filling and rupture of vessels which, having been rendered temporarily functionless owing to the pressure upon them of the contained urine, have undergone degenerative changes. In cases of chronic venous obstruction, *e.g.* by old inflammatory adhesions, tumour-growth, etc., the veins of the submucous coat of the organ occasionally become varicose, and, from their rupture, give rise to hæmorrhage.

CYSTITIS.—Inflammation of the mucous membrane of the bladder varies greatly in its intensity, minor degrees of cystitis being com-paratively common. The condition may occur alone, but is very often associated with pyelitis, urethritis, prostatitis, etc.

Causes.—Cystitis arises from the irritation of calculi, of new growth, or of the ova of *Schistosomum hæmatobium* (*Bilharzia*); but, in most cases, and even in those just mentioned, the condition is commonly due to bacterial infection. Bacteria may gain access to the bladder—

(*a*) **From below, by way of the urethra,** *e. g.* from the use of a dirty catheter, especially in cases of paraplegia and other paralytic diseases; or the bladder may become infected by the upward extension of a gonorrhœal or other form of urethritis. In the females, such ascending infection is specially common after defloration and parturition, and is mostly fre-quently due to *B. coli* and its relatives, with or without associated *Strepto-* or *Staphylo-cocci,* or to the *Gonococcus, Enterococcus,* etc.

(*b*) **From above, by way of the ureters,** for example, in suppurative or other infective diseases of the kidney.

It may here be noted that, in the kidney, bacteria may pass from the blood into the urine without any apparent gross lesion such as ulceration; and, in this way, bacteria, in some cases, reach the bladder. The presence of bacteria in the urine—**Bacteruria,** or, if due to bacilli, **Bacilluria**—does not necessarily, however, give rise to any special inflammatory lesions in the bladder or urinary passages. Bacteruria is very commonly present in typhoid fever, *B. typhosus* being passed, often in very considerable numbers; and, similarly, *B. paratyphosus,* and other members of the coli-typhoid group, *Micrococcus melitensis, Strepto-coccus rheumaticus*[1] and other organisms may occur in the urine in

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[1] Carnegie Dickson, working in conjunction with Dr. H. Moreland McCrea, Dr. A. Charles Gray and other clinicians, has isolated various streptococci—probably identical with, or forming a group closely allied to, the *Streptococcus rheumaticus*—from a series of some fifty cases of chronic rheumatic and rheumatoid arthritis, so-called fibrositis, muscular rheumatism, and allied conditions. In a large proportion of these cases, the joint- and other local lesions reacted in a specific manner to vaccines prepared from the streptococci so isolated.

cases of general infection by them. Another form of bacteruria, which is comparatively common, is that following a cystitis, pyelitis, or combination of these conditions, in which the inflammatory reaction gradually dies down but the organisms persist, sometimes in large, sometimes in small, numbers. Cases of this nature are very liable to relapses or recrudescences of the inflammatory condition when exposed to chill or other predisposing cause—a common sequence of events in, say, **B. coli bacilluria.**

(c) **By way of the blood- or lymph-stream.** The bladder may become infected from the intestine, through the weakened or damaged walls of which, organisms, e. g. *B. coli*, may pass and find their way by blood- or lymph-stream into the bladder. Such passage of organisms by these channels, however, probably takes place most frequently through the kidneys, as described above.

The bacteria most frequently found in cases of cystitis are the *B. coli* group, *Staphylococci*, especially *Staphylococcus pyogenes albus*, the *Gonococcus*, *Enterococci* and other forms of *Streptococci*, and *B. proteus*, as well as a number of bacteria whose classification is still doubtful. In many cases, such infections are **mixed** in character. Certain organisms which lead to alkaline decomposition of the urine may produce cystitis, a deposit of ammonium urate, phosphates, etc., being found on the mucous membrane. Except where this occurs, the urine, in cases of cystitis, is usually **acid** when passed, though it rapidly undergoes decomposition and becomes alkaline on standing.

Morbid Appearances.—The mucous membrane is congested, swollen, and usually thrown into folds. It is sometimes much discoloured, varying from dark-red to purple, and often shewing numerous extensive submucous hæmorrhages, the appearance sometimes almost suggesting that of gangrene. The surface may be covered by a red or yellowish-red deposit of precipitated ammonium urate, uric acid, earthy phosphates, etc., and the summit of the ridges with mucus, muco-pus, or, in some cases, with almost pure pus. The distribution of the inflammatory phenomena may be general, but is often more intense at the base or trigone. The openings of the ureters may be specially affected, particularly when there is associated pyelitis, e. g. they may shew congestion, œdematous swelling, hæmorrhage, etc.

Where the inflammatory condition becomes **chronic**, the bladder-wall may be greatly **thickened,** this thickening being due mainly to an overgrowth of fibrous tissue in the wall, though some degree of hypertrophy of the muscular coat may occur. Marked **contraction** may supervene, and, in some instances, the cavity of the bladder may be almost absent.

TUBERCULOSIS OF THE BLADDER.—*See under* **Genito-Urinary Tuberculosis,** p. 914.

NEOPLASMS OF THE BLADDER.—These are most frequently **papillomatous** in type—either simple, or, perhaps more commonly,

malignant in nature, the one group running into the other without any definite line of demarcation between them. They are characterised by the presence of masses of long, extremely delicate, branching villous processes, which consist usually of a scanty, highly vascular, connective-tissue core, covered by transitional stratified epithelium, very much resembling that of the normal bladder, though the superficial and more flattened cells may be absent. In simple cases, the condition is limited

FIG. 419.—*Villous Papilloma of Bladder*, composed of long, slender, branching processes with delicate vascular core covered by proliferated transitional epithelium.   ×200.

to the mucous coat, but, in those which are malignant, wide-spread infiltration may occur. All intermediate grades are found. **Hæmorrhages** from such tumours frequently occur, and small portions of the tumour may break off, and be found on microscopical examination of the urine.

Scirrhus tumours, though they may occasionally be primary, are more usually secondary, especially to tumours of the prostate; and the same holds good with regard to **adeno-carcinoma. Fibroma, myxoma, myoma,** and **sarcoma** are rare. **Cysts** are also very uncommon, but may originate from glands or from congenital defects connected with the urethra, urachus, Wolffian body, or Gärtner's duct.

MALAKOPLAKIA is an extremely rare condition which may attack the mucous membrane of the bladder—the authors having seen only two cases of it in twenty years. It is characterised by the presence of slightly-raised pale-whitish or yellowish-white opaque areas scattered over the surface, due to the development, mostly in the submucous coat, of masses of large polygonal cells, many of which contain clear rounded " Michælis-Gutmann bodies," staining deeply with hæmatoxylin, and being probably degeneration-products. The nature of the condition is still unknown, some writers having suggested that it may be neoplastic, granulomatous, or bacterial in origin, others that there may be more than one factor in its causation. This disease may also attack the kidney.

PARASITES.—The only parasite of importance which affects the urinary bladder is *Schistosomum hæmatobium* (*Bilharzia hæmatobia*), a full description of which will be found on p. 391. Carnegie Dickson (with Thomson Walker) has investigated two cases of urinary infection with **mites** (*see* pp. 440–1).

URINARY CALCULI

These are composed of certain normal or abnormal constituents of the urinary secretion which, either because of their excessive amount, or from precipitation owing to the occurrence of certain chemical changes—*e. g.* those found in decomposition of the urine—crystallise out, or are deposited in amorphous form. Such calculi may be composed of one, or, in many cases, of a mixture of two or more, of the following substances—**uric acid, urates, calcium oxalate, phosphates,** and, more rarely, **calcium carbonate, cystin, xanthin,** or **cholesterin.** In the calculus, these substances are bound together by an organic matrix, usually altered mucus or some similar substance, and may have a laminated, and frequently also a radially striate, structure. The " nucleus " of a calculus is usually composed of urates or uric acid (which may originate in the kidney) or, in some cases, may consist of a foreign body.

In Egypt and elsewhere, *Bilharzia* ova, or broken-off fragments of *Bilharzia* papillomata containing them, may form the nucleus of calculi.

Inflammatory, degenerative, and necrotic processes play an important part in the production of some calculi, *e.g.* inflammatory products may become infiltrated with the various chemical substances mentioned above. On the other hand, calculi, when once formed, act as foreign bodies, the irritation of which either helps to keep up a pre-existing inflammation, such as a pyelitis or cystitis, or predisposes towards its occurrence.

Calculi are single or multiple, and may lie free in the bladder, or be embedded in a diverticulum, or they may be impacted at the opening of the ureter.

Uric-Acid Calculi are formed where uric acid crystallises out in

consequence of excessive acidity of the urine, the acid phosphates using up some of the bases which should, under normal circumstances, be combined with it. This substance may also be precipitated where it is present in excessive amount because of dietetic and other errors; or where the watery part of the excretion is insufficient in amount to hold it in solution. Uric-acid calculi are hard in consistence, and more or less spherical or ovoid in shape. They are usually yellowish- or reddish-brown in colour, from the associated presence of urinary pigment. They are generally slowly formed, and may, if the urine becomes alkaline from decomposition, form the "nuclei" of more rapidly growing phosphatic stones.

Urate-Calculi, composed of ammonium or of sodium urate, etc., are rare. They are found chiefly in infants, though they also occur in adults from ammoniacal decomposition of the urine.

Calcium-Oxalate Calculi may originate in the pelvis of the kidney, and be carried down into the bladder. They are extremely hard, and usually present a rough, nodulated or "mulberry" exterior, by reason of which they give rise to considerable irritation and hæmorrhage, and are themselves generally stained a dark-brown or brownish-black colour, from the presence of blood-pigment. They frequently shew an admixture with uric acid, and they may form the nucleus of phosphatic concretions.

Phosphate-Calculi are found especially where there is ammoniacal decomposition of the urine due to bacterial infection. They are pale and chalky in appearance, soft, and friable, and are composed mainly of magnesium and calcium phosphates, usually mixed with varying quantities of calcium oxalate and ammonium urate, mucus, and urinary pigment. They are found commonly in cases of cystitis, when the urine becomes alkaline from decomposition, and they frequently exhibit a "nucleus" of uric acid. From the fact that it is fusible in the flame of the blow-pipe, the phosphatic calculus has been termed the **fusible calculus.** It is soluble in the mineral acids without evolution of gas.

Calcium-Carbonate Calculi, though common in herbivora, are rare in man. They are usually extremely hard, though soft forms may sometimes be found. They readily dissolve in a mineral acid, carbon-dioxide gas being given off.

Cystin-, Xanthin-, and **Cholesterol-Calculi,** are extremely rare.

DISEASES OF THE URETHRA

MALFORMATIONS.—Absence of the urethra, in whole or in part, may occur. **Doubling** of the channel, **abnormal communications** (e. g. with the rectum), **diverticula,** and other somewhat rare abnormalities, are occasionally found. The commonest and most important malformations are **hypospadias** and **epispadias.**

Hypospadias is a condition due to the non-closure of the floor of the urethra. All degrees of such non-closure may occur; and the anterior orifice of the complete portion of the channel may open at any point from the glans in front to the perineum posteriorly. In its most extreme form—the condition known as **pseudo-hermaphroditism**—the urethral opening is in the perineum; the scrotal integuments shew a central vertical cleft simulating the aperture of the vulva; and the penis is rudimentary and resembles a hypertrophied clitoris. The testicles may not have descended, or may be malplaced. In its lesser degrees, the anterior opening of the urethra is in front of the scrotum on the under aspect of the penis. In its commonest form, the deformity is slight, the aperture being on the under aspect of the glans in the position of the fraenum, which is imperfect or absent.

Epispadias is a condition where the urethral wall is defective upon the dorsal aspect of the penis. The opening may be on the upper aspect of the glans. More commonly, however, it is at the root of the penis under the symphysis pubis. In its most complete form, it constitutes part of the condition of extroversion of the bladder (*q. v.*, p. 919).

INJURIES OF THE URETHRA occur from lacerated wounds of, or, occasionally, from falls upon, the perineum—the passage, in the latter case, being " nipped " against the lower edge of the pubic arch. **Tearing of the urethra**—especially at or near the triangular ligament— is a common complication of fracture of the pelvic bones; whilst **false passages** may be produced by the unskilful use of the catheter in cases of stricture, etc., or the introduction of foreign bodies. These injuries are of importance from the fact that they produce **extravasation of urine** into the surrounding tissues, and also because any such injury may lead, later, to cicatricial contraction, and the production of **urethral stricture.**

INFLAMMATORY LESIONS.—The most important of these is the inflammation produced by the *Gonococcus* or *Micrococcus gonorrhœæ*. In the acute stage, the mucous membrane is red and swollen, and there is a glairy discharge which soon becomes purulent and usually slightly blood-stained. It contains numerous polymorphonuclear leucocytes, and also mononuclears and desquamated epithelial cells, in the interior of which—especially in the polymorphs—the causal organism may be found. The *Gonococci* penetrate deeply into the mucous membrane and the subjacent connective tissue, where they often persist for a long period. They may also infect the prostate, seminal vesicles, testicles, bladder, etc.; and, in the female, may produce gonorrhœal cervicitis, endometritis, salpingitis, or perhaps peritonitis. Secondary mixed infection with other organisms, especially *Staphylococcus albus* and diphtheroid bacilli, usually occurs comparatively early. Gonorrhœal urethritis usually persists as a chronic inflammation for a considerable period after infection, and is the commonest cause of stricture.

Other forms of urethritis occur, but are comparatively rare.

STRICTURE OF THE URETHRA may arise from cicatricial contraction following injury or inflammation.   It is most commonly gonorrhœal in origin.   The most frequent site of such strictures is at, or immediately in front of, the triangular ligament, *i. e.* at, or near, the junction of the membranous with the spongy portions of the canal.   From the resulting retention of urine, the urethra above the stricture, the bladder, and perhaps also the ureters and renal pelves, become dilated, and considerable hypertrophy of the bladder frequently ensues.

URETHRAL CALCULI.—These may be due to impaction from above, or, in some cases, primary.   In the latter case, they are usually phosphatic in nature, may be multiple, and sometimes attain to a considerable size.

TUMOURS OF THE URETHRA are rare.   Papilloma, fibroma, myoma, adenoma, cysts, carcinoma and sarcoma have all been described.   **Urethral Caruncle** in the female is a highly vascular tumour developing on the posterior wall of the urethra near the meatus.   It is covered by squamous epithelium.

These and allied conditions are more fully discussed in textbooks of Surgery and Gynæcology.

DISEASES OF THE GENERATIVE SYSTEM

In addition to its primary function of spermatogenesis, an important internal secretion is produced in the testis, probably by the so-called interstitial cells of Leydig lying between the gland-acini. Castration in the male child prevents the further development of the prostate and seminal vesicles and the special secondary sexual characteristics (development of hair on the face, and the male skeletal characters, enlargement of the larynx, etc.). Most of the ductless glands are affected in varying degrees, the thyroid being diminished, and the suprarenal cortex, pituitary and thymus increased, in size, with arrest of the normal retrogression of the last-named organ. The epiphyses remain longer unossified, and the bones tend to be thinner and more elongated than normal. In the **adult**, the prostate tends to atrophy, and the secondary sexual characters may become less marked. Very important effects upon metabolism are produced, and there is marked tendency to adiposity. These phenomena are due to the loss of the autacoid produced by the interstitial cells, and not to the absence of the sperm-producing tissue. Prolonged exposure to X-rays leads to atrophy, first of the seminiferous glandular tissue and, later, of the interstitial cells.

We do not propose to deal with the diseases of the female generative system, as these are fully described in works on Gynæcology [1]; or with various surgical affections, such as hernia, etc., for descriptions of which, textbooks of Surgery [2] may be consulted.

DISEASES OF THE TESTICLE

MALPOSITIONS.—The testes are developed within the abdomen, from which they should normally descend into the scrotum during fœtal life. **CRYPTORCHISMUS** or **UNDESCENDED TESTICLE** is the term applied to the condition where the descent has, either totally or partially, failed to occur. It may affect one or both organs, and the arrest may take place at any part of their downward course. Thus, the undescended testis may be situated within the abdomen, or in the inguinal canal. The organ is, as a rule, imperfectly developed and functionless as regards spermatogenesis, though the specific internal secretion is still usually produced by the interstitial cells, which are generally present. The condition is of importance from the increased liability of the gland to **injury,** or to become the seat of **inflammation** or **neoplastic growth.** In some cases, apparently from abnormalities in the attachments of the **gubernaculum testis,** the organ may find its way into the perineum or elsewhere.

[1] *Gynecological Diagnosis,* by Barbour and Watson, Green & Sons, Edinburgh and London, 2nd edition 1914; *Gynæcology for Students and Practitioners,* Eden and Lockyer, Churchill, London, 1916.
[2] *A System of Surgery,* edited by Choyce and Beattie, Cassell & Co., London, etc., 1915.

MALFORMATIONS and other congenital abnormalities occur : for example, the **non-development** of one or both organs, or, in rare instances, the occurrence of a **third testicle.**

HYDROCELE, or distension of the tunica vaginalis with fluid, may be **dropsical,** or, more commonly, **inflammatory** in origin. When of old standing, the tunica vaginalis may become much thickened. On the surface of the testicle this fibrous thickening may be irregular and nodular, and is liable to be mistaken, on naked-eye examination, for cartilage. In **congenital hydrocele,** the cavity of the tunica vaginalis remains in communication with the general peritoneal cavity. If hæmorrhage occurs into the tunica vaginalis, the condition is known as **HÆMATOCELE.**

ORCHITIS, or INFLAMMATION OF THE TESTIS, is produced by local infection by way of the urethra and vas deferens, as in **gonorrhœal orchitis;** or it may be due to a blood-spread, as in cases of **acute infective parotitis** or **mumps,** in which disease this complication is of not infrequent occurrence.

An orchitis commences usually in the epididymis, where it may remain localised, or from which it may spread to the body of the testicle. Acute hyperæmia and swelling occur, with or without extension of the inflammation to the tunica vaginalis. Recovery may take place, or the disease may go on to abscess-formation, or it may become chronic.

Chronic orchitis is characterised by fibrous overgrowth, with consequent atrophy of the glandular elements. It may, as just stated, originate in an acute attack, or it may be due to one of the chronic infective diseases, such as tuberculosis, syphilis, or leprosy.

TUBERCULOSIS OF THE TESTICLE.—The disease usually commences in the epididymis, and is due probably to a blood infection. The usual phenomena of the disease are seen, viz. caseation and fibrous overgrowth. These may, at first, be localised to the epididymis, which becomes palpable as an elongated firm mass, lying along the posterior border of the testis. The process tends to extend to the body of the gland, which, from the spread and coalescing of the caseous areas, may become entirely destroyed. Ulceration is liable to occur, with the formation of fistulous openings through the skin of the scrotum.

Reference has already been made to the tendency of the tuberculous process to spread to the bladder and kidneys (*see* **Genito-Urinary Tuberculosis,** p. 914).

SYPHILIS OF THE TESTICLE may take the form of a **diffuse chronic inflammatory overgrowth of the connective-tissue framework** of the organ : or of localised **gummatous** formation. In the latter case, the gummata may be multiple, and may, by their coalescence, cause practically total destruction of the gland.

TUMOURS OF THE TESTICLES.—**Simple tumours** are uncommon, the testicle being much more frequently the seat of malignant disease.

Cancers—especially those of the soft or encephaloid variety—and

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sarcomas may occur, the latter often exhibiting a mixed character, for example, combinations with myxomatous, chondromatous, adenomatous, and other tumours. Mixed cartilaginous tumours of the testicle are of special interest. They are sometimes highly malignant, and have been considered by some writers to arise from remnants or " rests " of aberrant and included vertebral cartilages—the testicle, before its descent, lying in close proximity to the bodies of lumbar vertebræ; they are now, however, believed by most authorities to be **teratomatous** in origin, this view being probably the correct one, there being usually an admixture of other tissues derived from the various embryonic layers present in such tumours in addition to cartilage.

Chorion-epithelioma is another tumour, of a teratomatous nature, which may occasionally occur in the testicle. In the male, it is necessarily a " tumour of consanguinity," *i. e.* derived from a germ-cell segregated very early in development and with potentialities in some ways resembling those of the impregnated ovum itself. In the male, such tumours are always of much greater malignancy than in the female, as, in the case of the latter, the tumour arises from the offspring, and the chorionic tissue may attain a varying degree of maturity, the resulting tumour shewing a corresponding variation in its malignancy—a lesser degree being found, the more mature the development of the tissue from which it originates.

Cystic tumours of the testicle sometimes occur, in which the testicle is transformed into a congeries of dilated cysts, originating possibly from the developmental intermingling with the remains of the Wolffian body or neighbouring structures.

DISEASES OF THE SPERMATIC CORD

Of these, the commonest is the condition of **VARICOCELE** or **varicose dilatation of the spermatic veins.** This occurs most commonly on the left side. (*See* under **Diseases of Veins,** p. 562.)

HYDROCELE OF THE CORD is due to distension of unobliterated remnants of the peritoneal diverticulum formed for the descent of the testicle, and from the lower part of which the **tunica vaginalis testis** originates. Hæmorrhage into these remnants, or into the tissues of the spermatic cord, constitutes the condition known as **HÆMATOCELE** or **HÆMATOMA** of the cord.

TUBERCULOSIS of the **vas deferens** may occur as part of the more widely spread condition known as **Genito-Urinary Tuberculosis** (*see* p. 914).

DISEASES OF THE PENIS AND SCROTUM

BALANITIS, or inflammation of the mucous membrane covering the glans and lining the prepuce, may occur independently; or it may be associated with the presence of hard chancre, soft sores, gonorrhœa, etc. Inflammatory affections of these parts are also found in some cases of gout and diabetes.

For descriptions of such conditions as **phimosis** (narrowing of the anterior orifice of the prepuce), **paraphimosis,** etc., reference should be made to textbooks of Surgery.

ULCERS, or **CHANCRES,** are of frequent occurrence, especially in the venereal diseases. **Hard chancre** is the primary lesion of syphilis, and is situated usually on the glans, either on the corona or in the neighbourhood of the frænum, and *Spirochæta pallida* may be found in a scraping from the base and edges of the ulcer, as well as in the juice of the enlarged inguinal glands obtained by puncture with a syringe. **Soft sores** or **chancroids** have a similar distribution. They have usually been regarded as due to local infection with Ducrey's bacillus, which may also be found in the buboes or enlarged lymphatic glands in the groin; but the specificity of this organism has not been clearly established. Soft sores—unlike the hard chancre—are not infrequently multiple. **Condylomata** or papilloma-like overgrowths also occur in syphilis. They may sometimes be of considerable size, forming masses somewhat resembling a bit of cauliflower in appearance.

TUMOURS.—The most important tumour of the **penis** is the **squamous epithelioma,** which originates usually in or near the glans, forming irregular, fungating, warty masses, which may undergo extensive ulceration. This form of tumour may also attack the **scrotum,** and, from its comparative frequency among chimney-sweeps, is sometimes called " **Chimney-sweepers' cancer,**" and is, at all events partly, due to the chronic irritation of soot-particles in this region.

ELEPHANTIASIS OF THE SCROTUM and **LYMPH-SCROTUM** are referred to on pp. 436–7.

DISEASES OF THE PROSTATE GLAND

The prostate gland may be affected by various **degenerative, inflammatory,** and **neoplastic** changes, the most important of these being the **enlargement** found very frequently in elderly subjects. This enlargement, often termed " **hypertrophy** " **of the prostate,** is, more accurately speaking, a **hyperplasia** affecting the muscular and connective tissue of the organ, with or without glandular proliferation. Where the gland-tissue shews proliferation, there is usually a marked tendency to the formation of numerous cystic spaces which may become filled with desquamated

epithelium, débris, and the so-called "amyloid bodies." The causes of this hyperplasia are obscure, and the overgrowth may sometimes almost resemble that of a tumour. The enlargement is, in some cases, a uniform one, but, very often, it is localised to some particular area of the gland, especially the central part, which may become enlarged and project into the cavity of the bladder at its neck, constituting the so-called "middle lobe" of the prostate. The prostatic portion of the urethra becomes elongated, and perhaps distorted and compressed, giving rise to **obstruction** to the outflow of urine from the bladder. This obstruction, from **superadded congestion,** may become "**acute**" or **complete.** Prostatic enlargement may, therefore, lead to **changes in the bladder,** resembling those produced by stricture of the urethra elsewhere, viz. **dilatation, hypertrophy, sacculation,** etc.

Wade [1] classifies the causes of **Prostatic Dysuria** or "**Prostatism**" as follows :—

Three outstanding varieties of disease lead to prostatism :

(a) **Prostatic Hypertrophy or Chronic Lobular Prostatitis,** the commonest lesion, present in 82 per cent. of his 134 cases. He considers the condition a senile hyperplasia, an aberrant growth of tissue that is not the result of the occurrence of an independent new growth, but is liable to develop into the same. It develops usually in the middle lobe, and is almost uniformly confined to the middle and lateral lobes. It is very rarely confined to the anterior lobe.

(b) **Prostatic Fibrosis or Chronic Interstitial Prostatitis,** present in between 7 and 8 per cent. of the 134 cases examined. The gland is reduced in size, and shews sclerosis of the interglandular fibrous tissue, with dense adhesions to the capsule.

(c) **Prostatic Carcinoma,** the commonest true tumour of the gland, and found in about 10 per cent. of his 134 cases. The three types of carcinoma in his series were **Scirrhus, Medullary Cancer and Adeno-carcinoma.** In Thomson Walker's series of 242 cases, 16·5 per cent. were malignant.

INFLAMMATION, or PROSTATITIS, may be **acute** or **chronic.** It is very frequently due to **gonorrhœal** infection, especially where stricture supervenes, but may also occur as a complication of certain of the acute infective diseases. In gonorrhœa, the infection reaches the gland usually directly by way of the urethra, either naturally, or assisted by injections or the passage of instruments. *Staphylo-* or *Strepto-cocci,* and *B. coli* are next in frequency to the *Gonococcus* as the infective agent. Diphtheroid, minute Gram-negative, and other, as yet unclassified,

[1] "Prostatism," by Henry Wade, *Annals of Surgery,* Philadelphia, Penn., March 1914, p. 321.

bacilli, are also common as organisms of secondary infection. The *Gonococcus*, though frequently the primary cause, is often masked or replaced by the other organisms named. In some cases, the disease is suppurative, and may occasionally lead to thrombosis of the neighbouring veins, and sometimes to pyæmia—a result which may also follow operative interference with the gland.

·**TUBERCULOUS DISEASE** of the prostate is not infrequent, especially as part of the condition known as **Genito-Urinary Tuberculosis** (*see* p. 914). The urethra, vesiculæ seminales, etc., may similarly be affected.

TUMOURS AND CYSTS.—Apart from the condition described above as hyperplasia, and which may sometimes closely resemble tumour-growth, neoplasms of the prostate are comparatively rare. **Fibromata** and **Myomata** may occur. **Cancers** constitute from 10 to 16·5 per cent. of carefully investigated series of prostatic cases operated on by the surgeon or examined *post mortem* (*see above*). 'Sarcomas are uncommon. Small **retention-cysts,** often filled with colloid material, are of frequent occurrence, especially in chronic lobular prostatitis.

PROSTATIC CALCULI AND CONCRETIONS in the ducts of the gland are of common occurrence in old persons. They are usually small, in size, and are due, as a rule, to infiltration of inspissated mucus with lime-salts.

DISEASES OF THE MAMMARY GLAND

CONGENITAL MALFORMATIONS.—Congenital absence of the nipple is extremely rare. **Absence** of one or of both breasts may occur, but is always associated with other developmental defects. **Imperfect development** is sometimes seen in association with similar defects in the genital organs. **Infantile hypertrophy** may be found during the first year of life— the mammary gland shewing an abnormal degree of proliferation of its glandular elements. **Abnormal development** is sometimes seen in the male breasts, especially about the age of puberty, and an imperfect secretion of milk occasionally takes place.

Supernumerary mammary glands are not uncommon, and are situated a little below, and internal to, the normal glands, in the region of the anterior axillary fold, in the middle line over the sternum, on the abdomen or in the groin, and, much more rarely, on the back, shoulders, arms, or other parts. These glands may be normal in structure and function; but, more commonly, they are rounded masses of mammary tissue without excretory ducts and without nipples.

The influence upon the mammary glands of the internal secretions of certain of the ductless glands is discussed in the chapter dealing with these organs.

ATROPHY supervenes as a **physiological** process after the menopause. Sometimes the atrophy is not associated with diminution in the size of the breast—an overgrowth of adipose, and even of fibrous, tissue replacing the atrophied glandular structure. **Pathological** atrophy is said to occur after removal of the ovaries in early life; but this change certainly does not take place in all cases of oöphorectomy.

HYPERTROPHY of all the constituent parts of the gland may develop at, or immediately following, the establishment of puberty—the changes produced being exactly comparable to those seen in the physiological enlargement of the lactation-period. Hypertrophy is also present in certain cases of ovarian and uterine disease. Osler and others describe cases of " hypertrophy "—or, more accurately, increase in size—of the gland in pulmonary tuberculosis, on the same side as the pulmonary lesion, and state that " the condition is one of chronic interstitial mammitis and is not tuberculous."

DEGENERATIONS.—Fatty and myxomatous degenerations are not common. The latter sometimes supervenes in areas of chronic fibroid mastitis or in fibromas.

INFLAMMATION :—

(a) **INFLAMMATION OF THE NIPPLE AND AREOLA** occurs most commonly at an early period of lactation. The parts become conical,

red, and swollen. Superficial ulceration, abrasions, and fissures, with a certain amount of sero-purulent exudate, are sometimes present. The condition is liable to cause infection of the breast and abscess-formation, which is often localised to the region of the areola but, in some cases, extends in the substance of the breast itself.

(b) A " CHRONIC INFLAMMATORY " condition of the nipple and areola was described by Paget, and was regarded by him as a precursor of carcinoma (see p. 937).

(c) ACUTE MASTITIS rarely occurs, except during the period of lactation; though it has been observed in infancy and childhood, at the time of puberty, and in the course of infectious diseases, especially in mumps. Such acute mastitis occurring during the period of lactation is usually due to infection from the nipple, the invading bacteria being commonly *Staphylococci* or *Streptococci*. The breast becomes swollen and hyperæmic, and the skin reddened. The inflammatory reaction may be widely spread or localised, and the process sometimes subsides without suppuration. Abscess-formation, however, is very apt to occur—the suppuration being confined to localised areas, or infiltrating widely. The pus tends to burrow in various directions, and may make its way into the ducts and be secreted with the milk, or may discharge externally through the skin. The abscess is situated in the sub-areolar tissue : in the breast itself: or in the tissues behind the breast—an abscess in the latter position being due, however, more usually to necrosis or tuberculosis of a rib or of the sternum, though, in some cases, it is produced by an extension of suppuration from the deeper parts of the breast itself.

(d) CHRONIC MASTITIS is usually divided into two main varieties— chronic interstitial mastitis and chronic lobular mastitis.

(1) Chronic interstitial mastitis is comparatively rare and, as a rule, only one breast is affected. The breast may be enlarged, and the nipple small and retracted. There is a marked increase of fibrous tissue, which is usually dense and non-cellular. The mammary ducts and acini are widely separated, and shew various degrees of atrophy. The fatty tissue of the breast is largely replaced by the newly-formed fibrous tissue. It is a matter of considerable difficulty to determine, in some cases, whether the process is of a chronic inflammatory, or of a neoplastic, nature.

(2) Chronic lobular mastitis, or chronic proliferative or productive mastitis, is a commoner condition than the foregoing, and both breasts are frequently affected. The changes are of a proliferative and degenerative character, and are seen especially in the lobules of the gland—involving both the acini and the interacinous connective tissue. The formation of cysts is extremely common; and, into these cysts, papillomatous epithelial ingrowths may take place. On section, the adipose tissue is scanty in amount and the glandular tissue more abundant than in the normal breast. The ducts are often dilated, and they, and also the cysts, may contain mucoid-looking

material, usually thin, and of a yellowish or brownish colour, in which cholesterol-crystals, in varying amount, are of common occurrence. Cholesterol-crystals are also occasionally deposited in the fibrous tissue itself in very old-standing chronic inflammatory cases. **On microscopical examination,** certain of the lobules may shew proliferative changes in the epithelium lining the ducts and acini, together with proliferation of the interacinous connective tissue. This new connective tissue is cellular, or densely fibrous. In other lobules, the epithelial proliferation is the principal morbid condition; whilst, in other there is a considerable degree of atrophy of the acini, with cystic dilatation as a result of compression and obstruction at some part of their course by the newly-formed fibrous tissue. According to Stiles, however, the majority of the cysts arise as a result of degenerative changes in the acini.

Circumscribed chronic mastitis is frequently met with, particularly in the axillary tail of the breast, and is due to prolonged lactation, or to injury of the breast. It exhibits the microscopical character of an interstitial, or of a parenchymatous (lobular) mastitis.

The various forms of chronic mastitis, especially those which remain localised, may—on account of the induration, the retraction of the nipple, and the period of life at which they usually occur—clinically closely simulate scirrhus cancer; and, in the cases in which the proliferative changes in the epithelium are a marked feature, the microscopical characters may come to resemble more or less closely, and indeed be indistinguishable from, those of a fibro-adenoma or of a scirrhus cancer. In the same breast, it is comparatively common to find varying **admixtures** of these lesions; and, in the opinion of the authors, scirrhus and other forms of cancer frequently supervene upon these so-called chronic inflammatory conditions, especially upon chronic proliferative or productive mastitis.

TUBERCULOSIS of the breast is comparatively rare, and is probably, in practically all cases, a secondary infection from a tuberculous focus elsewhere. The lesions are similar to those of tuberculosis in other organs and tissues—giant-celled follicles, with caseation, etc. Abscess-formation is said sometimes to occur as a result of the tuberculous infection. The axillary glands are affected in many of the cases. A "chronic interstitial, **non-tuberculous** mammitis" has been described as associated with pulmonary tuberculosis (*see* p. 934).

SYPHILIS.—The nipple and the areola are occasionally the seat of primary syphilitic lesions. These are sometimes multiple, and take the form of indurated sores, fissures, or ulcers, or there may be an indurated patch without ulceration. Secondary and tertiary lesions in the form of superficial ulcers, condylomata, and ulcerated gummata, are of commoner occurrence.

ACTINOMYCOSIS of the breast, as a primary condition, has been

described by some authors. Abscess-formation in the breast, secondary to intrathoracic actinomycosis, is also occasionally found.

TUMOURS AND CYSTS.[1]—These may, for descriptive purposes, be classified into those of the nipple and areola, and those of the body of the organ or corpus mammæ.

·A.—OF THE NIPPLE AND AREOLA :—

Tumours such as **myxomas, melanotic sarcomas, angiomas,** and **papillomas,** occur, but are very rare. **Epitheliomata**—especially the form known as **Paget's disease of the nipple**—are of greater importance.

Paget's Disease of the Nipple.—This somewhat rare condition, which is said to occur in about one per cent. of the cases of cancer of the breast, was described first by Sir James Paget, in 1874, as a disease of the nipple and mammary areola in some ways resembling chronic eczema, and almost invariably followed by cancer of the mammary gland itself. Most recent writers on the subject, with whom we agree, now regard the condition as carcinomatous from the outset, the condition apparently commencing as a slow-growing scirrhus cancer in the subjacent breast-tissue, and interfering with the normal lymph-drainage of the nipple by permeation or secondary fibrosis of the sub-areolar lymphatic plexus. **On naked-eye examination,** the earliest stage of the disease **resembles** a condition of chronic eczema of the nipple, with the formation upon it of small, dry, greyish, scale-like crusts, around and subjacent to which the tissues appear red and inflamed. The process gradually spreads circumferentially, first to the areola, and then to the adjacent skin of the breast. The surface becomes fissured and eroded, and bright red in colour. It may remain dry, scaly, and parchment-like; or, in other cases, there may be a viscid, clear-yellowish, or slightly-turbid, discharge. In the majority of his cases—to quote Paget's own words [2]—the patch "had the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of a very acute diffuse eczema, or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish viscid exudation. The sensations were commonly tingling, itching, and burning, but the malady was never attended by disturbance of the general health. I have not seen this form of eruption extend beyond the areola, and only once have seen it pass into a deeper ulceration of the skin, after the manner of a rodent ulcer.

" In some of the cases, the eruption has presented the characters of an ordinary chronic eczema, with minute vesications, succeeded by soft,

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[1] The classification and descriptions adopted in this section are based largely upon the work and writings of H. J. Stiles (see articles in *The Encyclopædia Medica,* vol. vii., Green & Sons, Edinburgh, 1901, p. 338, etc.).

[2] Sir James Paget, " On Disease of the Mammary Areola preceding Cancer of the Mammary Gland," *St. Bart.'s Hosp. Reports,* 1874, Vol. X., p. 87.

moist, yellowish scabs or scales, and constant viscid exudation. In some it has been like psoriasis, dry, with a few white scales, slowly desquamating; and in both these forms, especially in the psoriasis, I have seen the eruption spreading far beyond the areola in widening circles, or, with scattered blotches of redness, covering nearly the whole breast."

The nipple becomes indurated and retracted; and, later, as the process advances, it is destroyed. In the subjacent breast-tissue, there can generally be felt a hard mass of new growth, most commonly a slow-growing cancer of scirrhus type. This is usually palpable in from one to

FIG. 420.—*Paget's Disease of the Nipple.* See text. × 60.

two years after the appearance of the disease in the nipple; though, in some cases, it may not be so until later. For this reason, it was originally held that the condition of the nipple was of the nature of a chronic eczema, and merely predisposed and led up to the cancerous condition of the breast. It is probable, however, as already stated, that the condition is malignant from the first, and is a slow-growing carcinoma, commencing in the lactiferous ducts near their outlet, and gradually spreading to involve the surface, and also the deeper structures.

On microscopical examination, a vertical section through the affected areola shews areas of epithelial proliferation; and, especially in the deeper

layers of the epidermis, the presence of large, pale, rounded, or oval cells, with faintly staining protoplasm, and large, deeply-stained nucleus, usually single, but sometimes multiple—the so-called Paget-cells (see fig. 420). In the nipple, there is a similar condition, and also malignant proliferation of the cells lining one or more of the ducts, a condition which can be traced inwards and found to be continuous with the subjacent mammary tumour, which is usually of the ordinary scirrhus type. Enlargement and malignant infiltration of the glands in the axilla complete the picture of a scirrhus tumour.

B.—OF THE BREAST (Corpus Mammæ) :—

CYSTS.—Galactoceles, or " milk-cysts," may occur during pregnancy, but are of commonest occurrence during lactation. They are simply

FIG. 421.—*Intracanalicular Fibro-adenoma of Breast.* × 60.

retention-cysts, and are due to the usual causes, as in other glands, e. g. narrowing or obliteration of ducts or gland-acini by inflammatory changes, blocking by retained and inspissated secretion, etc. **Multiple small cysts** of similar origin are found in cases of chronic lobular mastitis (q. v., p. 936). **Involution-cysts,** due to distension of remnants of the glandular tissue during the retrogressive changes in the organ at, or subsequent to, the menopause, are not infrequent. **Parasitic cysts** such as **hydatids** are extremely uncommon, but definite cases have been described.

SIMPLE TUMOURS.—Pure fibromata occur, but are extremely rare. They exhibit the usual structure of similar tumours elsewhere. **Lipomata, myxomata, pure chondromata, mixed cartilaginous tumours** (osteo-chondroma, chondro-myxoma, chondro-sarcoma, etc.), and
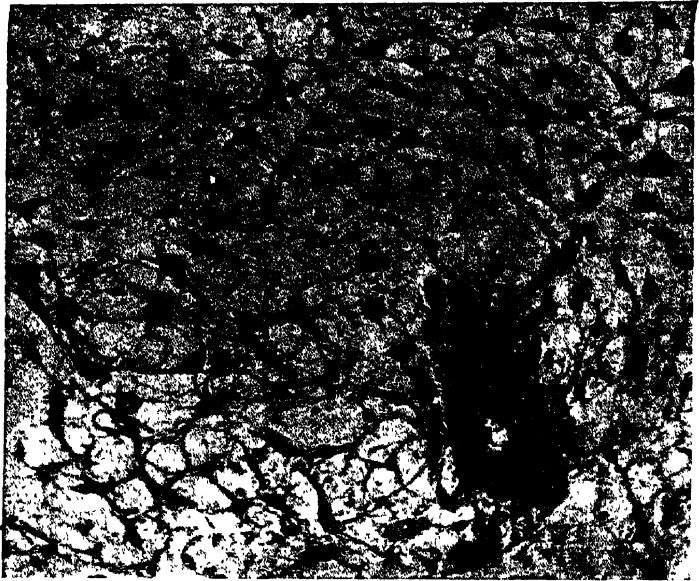
Fig. 422.—*Myxoma of Breast.* Shewing the characteristic branching cells. × 250.
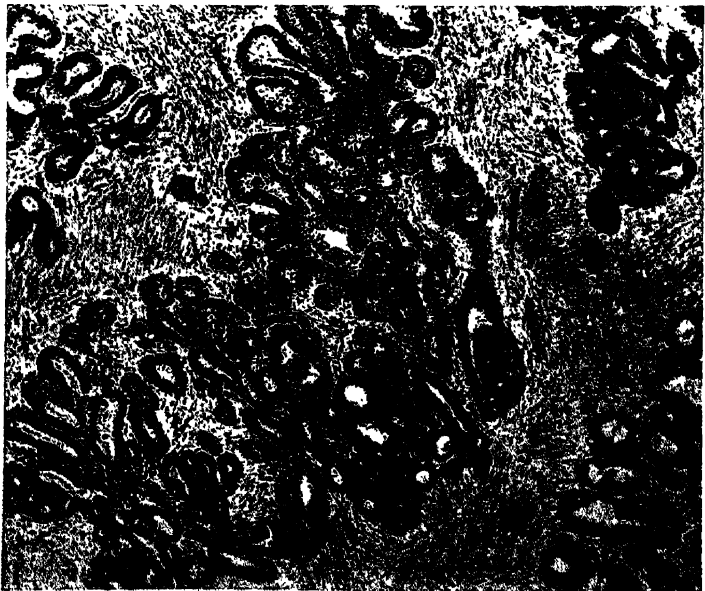
Fig. 423.—*Simple Fibro-adenoma* (or Fibro-Cystadenoma) of Breast. ×50.

angiomata, are likewise very uncommon, as are also pure adenomata of mammary gland-tissue. Fibro-adenomata, on the other hand, are common. Great variations are found in the relative amounts of the fibrous and glandular elements in such tumours, and also in their characters. Soft and hard varieties occur, the connective tissue in the former being abundant, highly cellular, and perhaps also myxomatous; whilst, in the harder varieties, it is scanty and more fibrous. Hard fibro-adenomata are, as a rule, small and slow-growing; whilst the softer varieties may be larger and—though usually also of comparatively slow growth—may sometimes grow more rapidly, especially on the occurrence of pregnancy. These

Fig. 424.—*Complex Adenoma (Papillary Cystadenoma) of Breast.* The acini are dilated and shew numerous papilliform ingrowths or infoldings. × 50.

tumours are definitely encapsuled, and do not infiltrate the surrounding tissues. On naked-eye section, the surface is dull white, or perhaps slightly pinkish in tint; and the cut surface usually bulges—a point of some importance in contradistinction to the retracted concave appearance of the cut surface often seen in sections of scirrhus cancers of the breast. It is often extremely difficult, and sometimes well-nigh impossible, to differentiate certain examples of fibro-adenomata from chronic mastitis with overgrowth of connective-tissue and irritative proliferation of the enclosed epithelial spaces and ducts; and it is very probable that many cases diagnosed as fibro-adenoma are in reality due to such chronic inflammatory proliferative changes. Cystic spaces may be developed in fibro-adenomata, the resulting tumour being known as a **cystic adenoma**

or **cyst-adenoma** of the breast. If the epithelium lining these cystic spaces grows more rapidly than the supporting connective-tissue wall, ingrowths may occur which, in section, resemble papillomata. These are often highly complex or branching in structure, giving rise to a foliaceous appearance of the tumour on naked-eye section. Such tumours, in some cases, attain a very large size, and are known as **proliferous cysts.** Extensive hæmorrhage may occur into their interior; their stroma is often myxomatous; and they may ufʼdergo extensive necrotic and ulcerative changes.

Duct-Papillomata are adeno-papillomatous ingrowths—often highly complex in their structure—which develop and come to project from the walls of one of the milk-sinuses or larger ducts near the nipple. ʻ The affected channel becomes correspondingly dilated, the contained mass of tumour being usually extremely vascular, and dark red in colour, and frequently giving rise to hæmorrhage, blood-stained fluid exuding from the nipple on squeezing.

MALIGNANT TUMOURS.—**Sarcomata** are much rarer than carcinomata, constituting, according to Stiles,[1] less than five per cent., and, according to Rodman,[2] less than three per cent., of breast-tumours. They are of the spindle- or round-celled—less commonly of the mixed-celled—type. Melanotic tumours of the breast are secondary to tumours arising in the nipple, areola, or elsewhere. These types of sarcoma do not call for further description, as, with regard to their appearance, methods of spread, etc., they resemble similar tumours in other situations.

Myxomatous degeneration may supervene in these tumours, as well as necrosis, hæmorrhage, etc.

Carcinoma is the commonest and most important neoplasm of the mammary gland. Its **relative frequency** is variously estimated by recent writers as about fifty to eighty per cent. of all breast-tumours. With regard to its **sex-incidence,** one per cent. or, at most, two per cent. of the cases of mammary cancer are in males. Women between forty and sixty—more particularly those between fifty-five and sixty—are most liable to the disease. We have already stated that, in our opinion, **there is a definite causal relationship between so-called chronic proliferative or productive mastitis and the various types of cancer.** In the great majority of cases, the cancer originates from the acinous epithelium, the main pathological varieties of such tumours being the **scirrhus, encephaloid,** and **colloid** types; whilst, in a certain proportion of cases, a glandular type of structure and arrangement in acinous spaces is maintained, the condition being then known as **adeno-carcinoma.** All intermediate forms between these main "types" may be found;

[1] Stiles, *loc. cit.*
[2] Rodman, *Diseases of the Breast,* Appleton, London, 1908, p. 162 (2·78 per cent. of sarcoma cases in a series of 5,000 cases of tumour of the breast).

and it is not uncommon to find different portions of an individual tumour exhibiting two or more—and even all—of these varieties of structure. Tumours which are typically scirrhus in their central or older portions, may be softer and more actively growing at their periphery, *i.e.* more encephaloid (or medullary) in type. Imperfect acinous spaces are of very common occurrence in certain parts of scirrhus and encephaloid growths; whilst colloid degeneration, though comparatively rare, may supervene in any variety of carcinoma. Histological descriptions of these tumours will be found in the Chapter on **Tumours** (p. 328 *et seq.*); and reference need be made here only to certain facts more particularly applicable to such tumours when occurring in the breast.
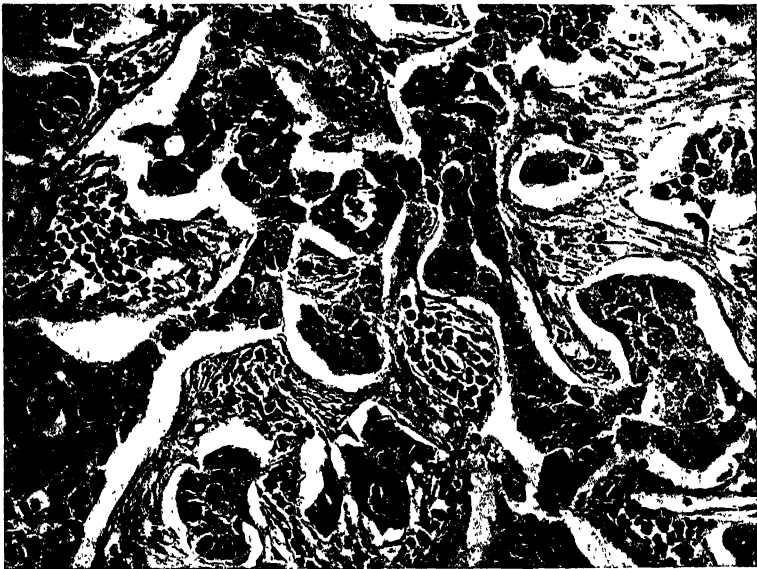
Fig. 425.—*Scirrhus Cancer of Breast.* Shewing solid masses of cells among dense fibrous tissue. (The clear spaces are artefacts due to contraction during fixation.)   × 200.

The most important malignant tumour of the breast is the **scirrhus** or **hard** variety of cancer (**spheroidal-celled cancer**). The ordinary nodular scirrhus tumour is a comparatively slow-growing neoplasm which may appear in any part of the organ. It is extremely dense, and, when palpated against the ribs, exhibits a "wooden," or almost "stony," hardness. The knife passes through it with a grating or creaking sensation, and the central, *i. e.* the oldest and densest, part of the cut surface, appears slightly concave, owing to the drag-ging of the contracted cicatrix-like fibrous tissue, which has a dull whitish appearance, sometimes mottled with yellowish areas of fatty degeneration. The spreading margin has a slightly more translucent, pearly white or, sometimes, greyish-pink appearance, and may show little red points of haemorrhage. Such growths may be " **circumscribed** "

or "nodular," or they may be "diffuse"; though, in either case, they do not shew any encapsulation, but spread by irregular processes into the surrounding tissue. The **nipple,** if the tumour be situated at or near it, tends to be **drawn up to a higher level than its fellow** of the opposite side, and to be **retracted** or drawn backwards into the breast (see fig. 426). As the tumour spreads, it infiltrates the neighbouring struc- tures—the **adjacent breast-tissue,** the **para- mammary** and **retro-mammary fatty areolar tissue,** and the subjacent **pectoral fascia**—pushing its way gradually into these along the lymphatic spaces and channels. The superficial layers of the **pectoralis major** and other subjacent structures are, in time, likewise invaded; and the infiltration may continue through the pectoralis major and come to involve the **intercostals, ribs, pleura, anterior mediastinum,** and **lung.** There may also be direct lymphatic spread to the **liver.** The overlying skin becomes invaded in the later or, in some instances, in comparatively early, stages of the condition. The spread takes place by way of the ligaments of Cooper, which pass from the skin into the breast. These become infiltrated and shortened, producing at first adhesion, then dimpling and puckering of the integument. The invaded area of skin may ultimately be destroyed by ulceration. At the same time, the cancer- cells spread, both continuously (by permeation) and also discontinuously (i. e. by a process

FIG. 426.—*Scirrhus Tumour of Breast.* Shewing dense bands of tumour-growth radiating from the nipple, which is retracted. The specimen has been treated with nitric acid (Stiles's method). The tumour appears dark, whilst the surrounding fatty tis- sue is pale in colour. (Edinburgh University Anatomical Museum. Catalogue No., Gen.-U. R. f. iv. 10.)

of malignant embolism), **along the lymphatic channels** which drain the breast area.[1] The majority of these lymphatics run outwards and upwards, accompanying the external mammary branches of the long thoracic artery, and opening into the pectoral group of lymphatic glands lying along the latter artery toward the anterior part of the inner wall of the axilla. Some of the efferent lymphatics from the breast also pierce the sternal portion of the pectoralis major muscle, along with branches of the internal mammary, and of the pectoral and long thoracic branches of

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[1] For detailed descriptions of the lymphatics of the breast etc., see papers by Stiles (loc. cit., and in *Brit. Med. Jour.*, June 17, 1899, p. 1452, and October 3, 1908, p. 971, and elsewhere); *Diseases of the Breast,* by Rodman, Appleton, London, 1908, p. 10; "Lines of Advance in the Surgery of Breast Cancer," by W. Sampson Handley, *Brit. Med. Jour.*, Jan. 8, 1921, p. 37.
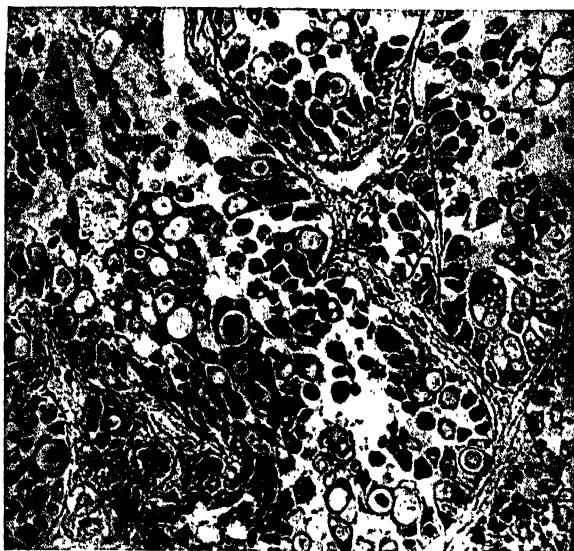
FIG. 427.—*Infiltration of Pleura by Scirrhus Tumour of Breast* which had assumed a softer type. The majority of the tumour-cells contain cell-inclusions around which clear digestive vacuoles are developed.   × 150.

FIG. 428.—*Tumour-Cells in Lymphatic Gland, secondary to Mammary Scirrhus Cancer.* These cells are larger than in the primary growth in the breast.   × 200.

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the axillary artery, and open into certain small lymphatic glands lying in the fascia on the deep aspect of the pectoralis major; whilst a few also open into the chain of sternal glands lying, within the chest-wall, along the course of the internal mammary. The infraclavicular, and certain other small, glands along the course of the superior thoracic artery may also be infected. Sampson Handley,[1] from the investigation of *post-mortem* material collated with clinical experience, emphasises the wide centrifugal spread of breast-cancer in the fascial lymphatic plexus, and notes its microscopic growing edge at points far removed from the breast: for example, in the deltoid region, or upper abdominal wall. The disease spreads from the affected axillary glands to those

Fig. 429.—*Scirrhus Cancer of Breast*, shewing the elongated clusters of tumour-cells among dense fibrous tissue.   × 75.

higher up in the axilla, and to the subclavian and supraclavicular glands, etc.; and complications due to pressure upon, and involvement of, the axillary vessels and nerves may supervene. Lymphatic infection of the inner ends of the first, second and third intercostal spaces, etc., and of the anterior mediastinal glands, sometimes follow. Metastasis may also—usually late in the disease—take place by the blood-vessels, and secondary growths occur in internal organs and elsewhere. Metastases in the bones, especially, it is said, of the cranium, vertebral bodies,[2] innominates, femur, humerus, ribs, etc., are compara-

[1] *loc. cit.*

[2] In a high percentage of their *post-mortems* upon cases of carcinoma of the breast, the authors have found such metastatic growths especially in the bodies of the dorsal and lumbar vertebræ. This is possibly accounted for by infection through lymphatics accompanying the intercostal vessels backwards towards the spine.

tively common. Infection of the other breast may take place along the intercommunicating lymphatics.

Certain forms of scirrhus tumour of the breast are extremely slow-growing and chronic. These **atrophic scirrhus tumours** are usually small, extremely hard, and fibrous; and their appearance on section has, from the presence of the dense white fibrous tissue intermixed with small yellowish points of fatty degeneration, been likened to that of an unripe pear, processes and strands of the growth radiating out into the adjoining tissues. **On microscopical examination,** the tumour-cells are scanty and degenerated, and are seen usually as small, compressed, elongated clusters, embedded in the dense fibrous tissue.

In some cases, these atrophic scirrhus tumours are diffuse, the whole breast being infiltrated and shrunken, and the nipple retracted and drawn upwards. Occasionally, the skin, not only of the breast itself, but of the surrounding thorax, etc., may be diffusely infiltrated—the so-called cancer " en cuirasse."

Encephaloid, Medullary, or Soft Cancer.—These are rapidly-growing tumours, to which the above names have been applied on account of their soft consistence. Other malignant tumours of the breast (e. g. sarcomas and adeno-carcinomas), however, resemble them so closely in naked-eye appearance that some writers object to these terms, and prefer to call them ." **Acute Cancers.**" They are extremely cellular, the cells being usually very irregular in size, and arranged in large solid clumps or masses embedded in a scanty connective-tissue stroma. They form large, soft, bulging, more or less circumscribed, masses, the so-called " **tuberous** " form; or they may be large, diffuse, tumours, rapidly infiltrating the breast and surrounding tissues—" **acute diffuse cancer.**" In both these varieties, the axillary glands are involved early, and metastases in other organs rapidly supervene.

Colloid or **Mucoid Cancer** is a slow-growing and comparatively non-malignant tumour, constituting from one to two per cent. of breast-cancers. Its characters are described in the Chapter on **Tumours** (p. 334).

Malignant Adenoma, including the so-called **Duct-Cancers** and the **Adeno-carcinoma** of Halsted.—**Duct-Cancers** proper are slow-growing and comparatively circumscribed tumours, consisting of tubular spaces lined by a single layer of columnar epithelium, or by several epithelial layers, the outermost of which is columnar. In some instances, these spaces become dilated to form cysts, perhaps with papillary ingrowths; though, sometimes, the lumen may be almost obliterated by the cellular proliferation. From the character of their epithelium, they are supposed to arise from the ducts.

Other tumours, which, from their association with the ducts of the organ, are sometimes included as " duct-cancers," have already been described, e. g. the carcinoma developing in Paget's disease of the nipple, which is usually an ordinary scirrhus cancer: and the adeno-papillomatous

ingrowths projecting into the lactiferous ducts and *cystic dilatations formed from these. These adeno-papillomata are probably simple tumours, and therefore need not be further discussed here.*

Adeno-carcinoma of Halsted.[1]—Halsted records the occurrence of five (possibly six) cases of this condition in a series of less than 150 cases of breast-cancer; and many other authorities (Stiles, Rodman, etc.) follow him in recognising the condition as a special type of tumour. **On naked-eye examination,** the tumours were large, soft, tuberous masses, with a tendency towards fungation or pedunculation (*i. e.* some constriction at the base of the tumour), necrosis, and ulceration. **On section,** they resembled encephaloid cancers; but an important point of difference between these two conditions was the non-involvement of the axillary glands in all of Halsted's cases—recovery following extirpation of the tumours, though these were of large dimensions—the axillary glands merely exhibiting endothelial hyperplasia.

On microscopical examination, these tumours are composed of very large tubules lined by epithelium many cells deep; and, in such a section, the cells have a tendency to form combinations such as—

" gland-like figures, circles, tubes, columns, and minute papillæ. The cells are often so snugly fitted together in these heavily-lined tubes . . . as to conceal the original figures; but almost always, even when the tubes are completely filled with tightly-packed cells, one can detect little circles of cells or little tubes which betray the tendency and the ability which the cells still have to form definite combinations." [2]

Occasionally, this form is found intermingled with areas of a more encephaloid or of a more scirrhus type.

For an account of the important **internal secretions** of the female generative organs, including the breast and the placenta, reference should be made to Schäfer's work on *The Endocrine Organs,* Longmans, Green & Co., London, 1916.

[1] Halsted, " A Clinical and Histological Study of certain Adeno-Carcinomata of the Breast," *Annals of Surgery,* Vol. XXVIII., July–December, 1898, p. 557.
[2] Halsted, *loc. cit.,* p. 562.

DISEASES OF THE NERVOUS SYSTEM

IT would be obviously impossible, within the limits of this textbook, to deal at all adequately with the pathology of the whole of the diseases of the nervous system. We therefore propose discussing only those diseases which are of comparatively common occurrence, and the pathology of which is more or less definitely established.

DISEASES OF THE BRAIN AND ITS MEMBRANES

The **dura-mater** forms the periosteum for the inner surface of the cranial bones and a definite connective-tissue membrane, in which the brain and spinal cord are enclosed. In this membrane, which is lined on its inner side with a single layer of endothelium, there is a vascular capillary network.

The **pia-arachnoid** covers the surface of the brain and cord, its deep layer following the various irregularities of, and being closely connected with, these surfaces. Between the dura and the pia-arachnoid, the subdural space forms a barrier, as it were, to the spread of inflammations from without or from within.

In the sulci between the convolutions, there is a loose connective tissue with many irregular channels in it—these channels constituting the **sub-arachnoid space.** Through the great transverse fissure, the pia-mater, with its contained vessels, is prolonged into the lateral ventricles, as the **velum interpositum** and the two **choroid plexuses.** Thus, there is a direct communication between the external covering of the brain and the internal ependymal lining of the ventricles.

There is also a communication between the ventricles of the brain and the sub-arachnoid space through the **foramen of Magendie,** and the **foramina of Luschke,** which are situated in the pial roof of the fourth ventricle. Thus, the sub-arachnoid space, the ventricles of the brain, and the canal of the spinal cord, form a directly continuous system of lymph-spaces in which the **cerebro-spinal fluid** circulates; but there is no similar direct communication between this system and the subdural space.

I. DISEASES OF THE MEMBRANES

CONGENITAL ABNORMALITIES, *e. g.* **Meningoceles,** etc. (*see* p. 965).

DEGENERATIVE CHANGES, of the nature of fibrous-tissue over-growth, associated frequently with thickening of the skull, and forming adhesions between the dura and the bone or between the pia and the dura,

and followed sometimes by calcification producing definite plaques, are seen in the dura- and in the pia-mater in old people, in the insane, and in alcoholics.

Sometimes, the thickening, particularly of the pia-arachnoid, is widely spread; or localised fibrous areas, especially at the points of intersection of the sulci, are produced, and may be mistaken for tubercle-granulations. If examined closely, however, their edges are seen to be rather indefinite, merging more or less gradually into the surrounding tissue. When distributed in a more patchy manner, they resemble the cloudy appearance of early purulent meningitis, but, usually, can be distinguished from the latter by their more peatly white lustre. In chronic forms of insanity, especially **paralytic dementia,** there is generally thickening of, and adhesions between, the membranes themselves, and also between the membranes and the cortex. The ependyma of the ventricles is thickened, and there may be papillary overgrowths into the cavities. The choroid plexuses may also shew chronic thickening, and an accumulation of " brain-sand."

· .The **Pacchionian bodies,** which are villous projections of the arachnoid, and the functions of which are not definitely known—though some authors consider that they are concerned in the lymph-return from the brain— are often more numerous than normal, and sometimes project into the wall of the superior longitudinal sinus.

THROMBOSIS OF THE CEREBRAL SINUSES, which frequently arises from disease of the dura-mater, may be " simple " or **septic.** The thrombi may arise as a sequel of acute fevers, in wasting diseases (" **marantic** " **thrombi**), or in certain blood-diseases, and are found in the superior **longitudinal sinus,** commencing at the anterior part and spreading backwards as far as the **torcular,** in the **lateral sinuses** and in the **cavernous** and **circular sinuses.** In the two latter positions, however, the thrombi are generally the result of pressure on the sinuses by tumours of the pituitary body or of the sella turcica, or of syphilitic disease of that part of the dura-mater forming the walls of the sinuses. In the **lateral sinuses,** the thrombi are most commonly septic, and arise usually by the spread— directly through the bone or by way of the **petrosal sinus**—of infective material from the middle ear, with or without necrosis of its bony roof. From the lateral sinus, the condition may spread down the internal jugular vein. Thrombosis of the **straight sinus** and of the **veins of Galen** is of considerable importance, from the fact that, by these channels, blood is returned from the interior of the brain and the basal ganglionic region. The thrombi may also result from traumatism.

If the thrombus is non-septic, it may produce venous congestion and rupture of small vessels on the surface of the brain, thus giving rise to haemorrhages. If, however, it is septic, the clot may become softened and fragmented, the walls of the sinuses be destroyed, suppuration supervene, and pyaemia result.

MENINGEAL HÆMORRHAGE :—

1. **Pachymeningitis Hæmorrhagica.**—This lesion is seen as a mass of blood-clot more or less adherent to the inner surface of the dura, and covered, on its inner surface, by a thin membrane. This membrane is generally of a brownish colour—evidently from the presence of the colouring matter of the blood—and extends, as a thin soft layer, to the surface of the dura, with which it is continuous beyond the clot.

By many authors, this disease is said to commence as a slowly-developing inflammation of the dura-mater, characterised by hyperæmia. A soft membrane, containing spindle-shaped and stellate cells, and having large thin-walled vessels, is formed; and, from these vessels, hæmorrhage occurs into the membrane. Some writers, however—and with these we agree—maintain that **hæmorrhage into the dura,** or, more usually, **into the subdural space,** is the primary condition, and that the membrane is a later production, arising by proliferation of the endothelial lining of the dura-mater—a process analogous to that seen in the isolation of thrombi in vessels. From the dura-mater, vessels, accompanied by connective-tissue corpuscles, pass into the clot, and organisation takes place—the whole being eventually converted into fibrous tissue, which coalesces with the dura-mater. During the early stages of this process of organisation, the young vessels may become dilated and may rupture, and thus fresh hæmorrhages may occur. The stellate and other cells which are seen in the clot are the cells of the organising tissue.

Recurrent attacks of the disease are common, and thus several layers, in different stages of transformation, may be found at one time, and a laminated cystic condition be produced.

The hæmorrhage may be traumatic in origin, and secondary to vascular or other degenerations in some forms of insanity, epilepsy, and in chronic alcoholism; or it may be found in such diseases independently of traumatism. It is usually confined to the dura over the convexity of the brain.

2. **Hæmorrhage into and on the Membranes.**—Hæmorrhages in the membranes of the brain, as primary conditions, are of minor importance. In acute meningitis, in septicæmia, in scurvy, etc., small hæmorrhages take place into any of the membranes; whilst, in anthrax, "the brain may exhibit no conspicuous lesion, or there may be extensive hæmorrhages into its substance or in the membranes." [1] Injuries of the skull, or injuries and hæmorrhages of the brain, sometimes secondarily involve the membranes, and give rise to hæmorrhages into them. In such cases, blood may be found between the skull and the dura-mater, in the subdural, or in the subarachnoid, space. These hæmorrhages may be caused by penetrating wounds of the skull; by simple contusions of the skull,

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[1] Spear and Greenfield, "Woolsorters' Disease," *Local Government Board Medical Officer's Report*, 1880, Appendix A, No. 8, p. 77.

and are found in cases of concussion due to the bursting of shells and other forms of explosives without any external wound. Such hæmorrhages may be extra-dural, or in the sub-arachnoid space. Similar hæmorrhages are found in some cases of tuberculous, and of cerebro-spinal, meningitis.

INFLAMMATION—MENINGITIS :—

1. **PACHYMENINGITIS.**—The inflammations of the **dura-mater** are usually **secondary** to injury or disease of the sinuses or of the bones of the skull. Thus, they may be caused by **traumatism,** by **tumours** growing from the bones of the skull or invading the cranial cavity by perforation of the bones or by passage through the foramina, by **gummata** of the skull as well as of the dura itself, and by **suppuration** extending from the bones of the middle ear either directly or by way of the lateral sinuses. **Caries** or **necrosis of bone,** the result of tuberculosis or of syphilis, may also give rise to inflammation; and syphilitic meningitis occurs without gummata and without necrosis of bone

. **Effects of Septic Pachymeningitis.**—When the outer part of the dura alone is affected, the membrane is swollen and dark red or greenish in colour, and may become separated from the bone by extra-dural collections of pus. On the inner surface, there may be a thin layer of greenish-yellow lymph. When the disease has reached the inner surface of the membrane, the spread is more rapid and more extensive. The pia-arachnoid is usually affected, and purulent effusion is present in the subdural and the sub-arachnoid spaces in the meshes of the pia-arachnoid and in the sulci. Granulation-tissue is developed, and adhesions may form between the pia-arachnoid and the dura.

2. **LEPTOMENINGITIS, or Inflammation of the Pia-arachnoid.**—The term **meningitis,** in its ordinary use, is often applied to inflammatory changes in the pia-arachnoid, probably because leptomeningitis is far commoner than are inflammatory affections of the dura.

Ætiology.—Leptomeningitis may occur as a primary infection, though the channels by which the infective material gains entrance are often obscure; but, in many cases, the **blood-stream** must be regarded as the principal carrier. Other routes of infection, however, are the **lymphatic channels** and the **lymphatic spaces** in the areolar tissue. Direct entrance from the ear, or from the nasal cavity and its accessory sinuses, is probably a not uncommon means of infection. The condition may occur also as a direct spread from inflammatory foci in the dura-mater or from the brain itself, as in "**epidemic encephalitis**"; it may arise, either primarily or secondarily, in the **acute infective diseases,** e.g. in influenza, in pneumonia, and as a sequel of measles, whooping cough, typhoid fever, etc., or during an attack of acute rheumatism, in Bright's disease, or in the course of any form of tuberculosis. It has been described by some authors as occurring in mumps, but it

should always be remembered that meningeal irritation, giving rise to symptoms very closely simulating, if not identical with, those of meningitis, is not uncommon in pneumonia, measles, mumps and other diseases, without any cytological or bacteriological evidence of meningitis. This condition is now usually called " **Meningismus.**" The commoner causal organisms of meningitis are *Pneumococci, Streptococci, Staphylococci, Meningococci, B. pneumoniæ, B. typhosus, B. influenzæ, B. tuberculosis,* etc. Certain *Leptothrix*-like forms have also been isolated in a few cases; and one of the authors (W. E. C. D.) has isolated *B. paratyphosus B.* in three cases of suppurative meningitis in young children.

Pathological Anatomy.—Excluding, for the present, the specific cases due to *Meningococcus* and *B. tuberculosis,* which will be described separately, leptomeningitis, in the early stages, gives rise to a rosy-red colouration of the pia-arachnoid. The vessels are much distended, and there may be hæmorrhages. Later, a slightly turbid inflammatory exudate, which is generally bilateral and often symmetrical, is seen, especially along the lines of the vessels. This fills up the sulci and obscures the convolutions, and, later, may shew as a thick, somewhat gelatinous layer on the surface of the brain. The exudate may become purulent, and, in severe cases, the sub-arachnoid space is filled with pus. The cerebro-spinal fluid is increased in amount, turbid, and even purulent. The cortex shews marked hyperæmia, and this inflammatory hyperæmic condition sometimes spreads inwards along the superficial vessels, constituting an encephalitis. Occasionally, large areas of softening or small abscesses are found in the substance of the brain. **On microscopical examination,** the softened areas of inflamed brain-substance shew dilatation of the minute vessels, and early degenerative changes in various nerve-cells.

The meningitis may be **localised** or **diffuse,** and attempts have been made to classify the various forms according to their situation, and by the character of the exudate. Thus, it is claimed that the exudate in pneumococcal infection is thick, viscid, and greenish in tint; while that due to the *Streptococci,* the *Staphylococci,* etc., is more fluid or serous, and paler in colour. Again, it is said that the pus is most marked at the **base of the brain** in those cases which are secondary to diseases of the middle ear, etc., or where the inflammatory process has spread upwards from the spinal cord; while, in those in which the infection is carried by the blood, the exudate is most marked at the vertex. Though these differences are present in certain cases, and may be useful as rough guides in *post-mortem* diagnosis, too much reliance must not be placed on them.

3. **EPIDEMIC CEREBRO-SPINAL MENINGITIS.**—This form of meningitis occurs generally in epidemic form, but sporadic cases are not uncommon. The disease has been of frequent occurrence among young recruits and seems to be associated especially with overcrowding, *e. g.* on board transports, in barracks, and in crowded camps. The organism

concerned is *Meningococcus* or *Diplococcus intracellularis meningitidis* *(Weichselbaum)*. This organism, which is most commonly intracellular, is found in the cerebro-spinal fluid, and one of the authors has found them in large numbers in the intraventricular fluid. At least four **types** of the organism, differing slightly from one another in their immuno-logical characters, have been described. It is found, in some cases, in the peripheral blood, and, more rarely, in the urine and other situations such as fluid from joint§, discharge from the ear, sputum in cases of broncho-pneumonia, etc. The organism is found in the naso-pharynx in some apparently healthy people, in those who have been in close contact with definite cases, and in patients who are suffering from the disease. Among these, a certain proportion are " **carriers,**" and it is sometimes very difficult to get rid of the organism, partly owing to pathological changes in the naso-pharynx. (These changes are referred to under the **Respiratory System, p.** 662.)

The pia-arachnoid, in the early stages of the disease, shews evidence of hyperæmia and serous exudation with the presence of a few leucocytes and red corpuscles; but later, if the patient survives, the exudate becomes purulent, and the pathological picture resembles that seen in pneumo-coccal and other forms of leptomeningitis. The exudate is found in the sub-arachnoid space, especially in the sulci between the convolutions on the upper surface of the cerebrum, in the fissure of Sylvius, and on the surface of the pons and medulla, and the upper surface of the cerebellum, though usually it is most marked at the base posteriorly. According to Stuart M'Donald,[1] the exudate specially accumulates in the posterior arachnoid cistern. Most authors state that, very frequently, the infection, even in the early stage, spreads along the prolongations of the pia-arachnoid into the ventricles.[2] Accumulations of serous fluid, with inflam-matory cells and numerous cocci, occur, giving rise to **hydrocephalus,** this, no doubt, being also due, in part, to an interference with the drainage by the various openings which normally establish communication between the lateral ventricle and the general sub-arachnoid space. The brain-tissue forming the walls of the ventricles, as well as that of the surface, becomes injected, œdematous and even infiltrated with inflammatory products **(acute encephalitis).** Hæmorrhages may occur into the brain-substance, and, in some cases, the cerebro-spinal fluid consists of almost pure blood and contains very few inflammatory cells. An acute **leptomeningitis,** of the spinal membranes is present, and a diagnosis may generally be made during life by finding the characteristic organism in the cerebro-spinal fluid obtained by lumbar puncture. **Herpes** is common on the lips, and a hæmorrhagic **petechial rash** is frequently present. The hæmorrhages may

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[1] Stuart M'Donald, "The Pathology of Epidemic Cerebro-Spinal Meningitis," *Review of Neurology and Psychiatry,* Aug. and Sept. 1907, p. 610.

[2] One of the authors (W.E.C.D.) is strongly of opinion that the direction of this spread is frequently, if not almost always, in the **opposite** direction, *i.e.* **from** the ventricles outwards to the surface (*see* p. 955).

be only few in number, or very wide-spread and very numerous. In some cases, the subcutaneous hæmorrhages are of large size. **Pleurisy, pericarditis,** and **parotitis** are not uncommon as complications. **Pneumonia,** either of lobar, or of broncho-pneumonic, type, may occur in association with this form of meningitis. **Arthritis,** with a serous or a purulent exudate, is common, and some of the cranial nerves are not infrequently involved directly in the inflammatory process. Of these, the optic nerve, is perhaps the most commonly affected, with resulting **acute papillitis** or **optic neuritis.** The third, and, occasionally, the sixth, nerve is involved. The inflammation may spread directly into the eye along the pia-arachnoid of the optic nerve, causing **choroido-iritis** or **keratitis,** and, in some cases, an inflammatory affection of the fifth nerve causes keratitis and **purulent conjunctivitis. Deafness** is not uncommon, and, in most cases, is due to inflammation of the labyrinth or of the eighth nerve in the internal auditory meatus. Later, **otitis media** and involvement of the mastoid cells may occur. According to some observers, the spinal infection is sometimes a sequel of the severe enteritis which has been described in some of the cases—the infection passing to the spinal cord by way of the lymphatics. We have never seen any evidence of this.

From the *post-mortem* examination of over a hundred fatal cases of cerebro-spinal meningitis occurring during the war, Carnegie Dickson found that the ventricular system is the site of acute inflammatory changes —often as, or even more, marked than those in the meninges. Turbid fluid containing large numbers of inflammatory cells was present in every case, in varying amount, according to the degree of acute inflammatory hydrocephalus. There was usually a copious deposit of somewhat soft fibrino-purulent material upon the ventricular walls, especially in the more dependent parts, such as in the horns of the lateral ventricles and in the third ventricle and infundibulum, the latter as well as the former cavities generally shewing distension. The ependymal lining of the whole chain of ventricles shewed swelling, and there was commonly softening of the neighbouring brain-tissue—an acute encephalitis often with hæmorrhages, generally small or petechial, but not infrequently considerable in size, and sometimes so extensive, as to bring about ploughing up of the cerebral substance. In some cases, the blood burst into the ventricles and extended down into the membranes of the cord, and was diagnosed during life by lumbar puncture. Periventricular encephalitis appears to be one of the most important factors leading to a fatal issue, especially where it involves the structures in the floor of the fourth ventricle. From his examination of this series, Carnegie Dickson is of opinion that, in these fatal cases at all events, although it is difficult by *post-mortem* evidence alone to be certain of the direction of spread, the infection of the ventricles had usually preceded that of the meninges, the organisms having been carried from the naso-pharynx or accessory nasal sinuses, to the choroid plexuses by the blood-stream, and setting up an **endo-ventriculitis** or

ependymitis. In very acute cases, with a rapidly fatal issue, the ventricular inflammation was usually more obvious than that of the meninges, which sometimes shewed no naked-eye changes beyond acute congestion.

In practically all cases, meningococci were more numerous in the ventricular, than in the spinal, fluid, and were present sometimes in large numbers in the former in cases where they could not be detected in the lumbar-puncture fluid. From the ventricles, the infection appears to spread to the surface of the brain especially at three points, viz.: (1) through the thinned and inflamed floor of the third ventricle and infundibulum, and so comes to be specially abundant in the cisterna basalis round the pituitary stalk, from the optic commissure in front to the crura and pons posteriorly; (2) through the pial roof of the fourth ventricle and its foramina, to the surface of the medulla and under aspect of the cerebellum, etc.; and (3) backwards, through the great transverse fissure, to the central lobe and culmen of the cerebellum and the neighbouring parts, and sometimes through the valve of Vieussens or superior medullary velum. The surface exudate is usually found especially over these three areas. From these it may spread and coalesce, giving the typical "basal" or rather "post-basal" distribution, and, later, it extends down the cord, and, to a varying degree, over the surface of the cerebellum and cerebrum. The exudate appears to be very much less liable to spread forwards over the cribriform plates of the ethmoid, round the olfactory tracts and bulbs, a point which appears to militate against the view, put forward by some, that the infection spreads to the brain through the roof of the nose and cribriform plate. In three cases in which the ventricles were tapped during life, the ventricular fluid was found to contain more inflammatory cells and meningococci than the lumbar-puncture fluid—in two of these, and in a number of the *post-mortem* cases, the organisms were so numerous as to resemble a "cultural" growth. In some cases, this ventricular infection seems to persist after the surface condition has cleared up under serum-treatment, a fatal issue may occur, the cord may be found "clean" at the *post-mortem*. In other cases which have cleared up, but in which the foramina in the pial roof of the fourth ventricle have become blocked, a non-inflammatory or retention-hydrocephalus may ultimately supervene and cause death. Another phenomenon which aids mechanically in the production of hydrocephalus is the pushing down of the medulla and the adjacent portions of the cerebellum into the foramen magnum, compressing the foramina in the pial roof of the fourth ventricle, and preventing the egress of fluid even when these foramina are not blocked by exudate. Such driving down of these structures into the foramen magnum, like a cork into the neck of a bottle, may be produced both by the congestion and swelling of the whole brain, and by the accumulation of fluid in the ventricles, *i. e.* this condition and the hydrocephalus, however produced, aggravate one another.

4. POSTERIOR BASAL MENINGITIS.—In this condition, the exudate, though sometimes extending to the vertex of the brain, is usually confined to, and always most marked at, the base. The exudate is more or less gelatinous, and is often most marked in the posterior arachnoid cistern. In the spinal cord, all degrees in a purulent leptomeningitis are met with. It is said that the onset of the disease is not so sudden as is that of the epidemic cases, and its duration is more protracted; yet acute, rapidly fatal, and epidemic cases of posterior basal meningitis occur. A diplococcus, which he considers specific for this disease, has been described by Still; but, by most authorities, this organism is regarded as merely a modification of the *Diplococcus intracellularis meningitidis*. Work by Gordon and others has shewn that, as has been pointed out on p. 954, at least four types of *Meningococci* can be identified by serological reactions, and that, among these, there are distinct variations in regard to virulence. In our view, posterior basal and epidemic cerebro-spinal meningitis are merely varieties of the same disease, the difference depending, in part at any rate, on a variation in virulence of the *Meningococcus*. Much evidence has been recently brought forward in support of each view, but, as this is concerned almost wholly with the **bacteriology** of the conditions, we do not propose to discuss it here.

5. TUBERCULOUS MENINGITIS is very common, and, though seen most usually in children and young adults, it may occur at any age. In the vast majority of cases, the inflammatory process—within the skull, at all events—first becomes evident at the base of the brain. In the early stages, the exudate is limited to the interpeduncular space and the area around it, but, eventually, it spreads to parts in continuity with these—**backwards** over the upper surface of the cerebellum: **laterally** along the Sylvian fissures: and **forwards** between the hemispheres and over the corpus callosum: and also into the substance of the brain along the connective-tissue sheaths of the vessels at the perforated spots. Thus, the condition may involve a very considerable surface area of the brain, extending even to the vertex. In the early stages, the exudate may be only slightly turbid and opaque, but, later, it becomes somewhat yellowish or greenish in colour. It is never definitely purulent. Tubercle-granulations are present in the membranes, but, in early cases, they may be so minute as to be almost invisible to the naked eye. Sometimes, they are better seen along the vessels in the Sylvian fissures and along the arterial branches which have entered the brain-substance at the perforated spots, than at the base, but, in all doubtful cases, the membrane should be viewed under a low power of the microscope.

On examining the brain *post mortem* the convolutions are usually flattened, and the pia-arachnoid is somewhat dry and glazed. The exudate and the minute tubercle-granulations, already referred to, may be seen. On making a section of the brain, the ventricles are found to be distended with a clear or, more usually, a somewhat turbid fluid, the amount of

distension varying greatly, and being most evident in the lateral ventricles, round which the brain-tissue is softened. This softening may extend somewhat deeply, and is probably a result of maceration by the accumulated fluid, or of obstruction to the vascular supply by pressure. The choroid plexuses contain tubercle-granulations. A diffuse encephalitis, sometimes of a hæmorrhagic nature, may be associated with the tuberculous meningitis. The appearances at the base of the brain have been described. The exudate may surround the nerves at the base of the brain and give rise to neuritis.

The pia-mater of the spinal cord is very commonly affected, and, in our experience, it is exceptional to find a tuberculous meningitis which does not affect both the brain and the cord. In the majority of cases, according to Greenfield, the cervical region of the spinal cord is first affected, possibly by way of the lymphatics from the thorax or abdomen—the condition then spreading both upwards and downwards, and, in its upward spread, extending along the "medulla oblongata to the base of the brain. In many of the cases which we have examined, the process was most advanced at the cervical region of the cord, and we think that, in a large number of cases at all events, there is a considerable amount of evidence to support Greenfield's view. The fluid in the ventricles may be very considerable in amount, and give rise to **acute hydrocephalus.** In most cases, this accumulation is due to an occlusion of the communications between the ventricular system and the subarachnoid space by the inflammatory changes in the region of the fourth ventricle; but it is also sometimes produced by an extension of the inflammatory processes along the choroid plexuses.

Microscopical examination of the exudate shews that, in most cases, the cells present are mainly mononucleated—**lymphocytes,** or cells of the lymphocyte-type. In some cases, however, and especially in those which run a very acute course, considerable numbers of **polymorphonuclear leucocytes** are found. *B. tuberculosis* may be present in very small numbers and may be discovered only after prolonged search. Polymorphonuclear leucocytes are a marked feature in some cases re-examined a day or two after the previous withdrawal of cerebro-spinal fluid. The appearance of large numbers of polymorphs is also apparently an almost constant feature in those cases of tuberculous meningitis which have been erroneously diagnosed as cerebro-spinal fever, and into the spinal theca of which anti-meningococcic serum has been injected—a similar phenomenon occurring from the intrathecal injection of anti-meningococcal serum into cases of cerebro-spinal syphilis. The cell-picture so produced by such injection of serum into tuberculous or syphilitic meninges may, therefore, closely simulate, and be mistaken for, that of true acute cerebro-spinal meningitis. *Meningococci*, however, will necessarily be absent. **Lymphocytosis** in the cerebro-spinal fluid suggests tuberculous meningitis but meningeal symptoms or actual meningitis may occur in mumps, in measles, in syphilis, etc., and, in these conditions,

lymphocytosis is also a marked feature. Lymphocytosis is also seen in general paralysis of the insane, which is now regarded as syphilitic in origin, and in other manifestations of disease of the brain and membranes.

Tuberculous masses or **nodules** in the brain-substance are found in some cases of tuberculous meningitis, but these will be referred to under **Tuberculosis of the Brain** (p. 985).

. **Methods of infection.**—The disease is frequently part of a general tuberculosis, the primary seat of infection being, in many cases, in the bronchial, cervical, or mesenteric glands, and the infective material passing to the meninges by way of the lymph- or the blood-stream. Again, the infection may start from a local tuberculosis of the brain, as, for example, a tuberculous nodule; or spread from tuberculosis of some of the bones of the skull or of the vertebral column. A tuberculous focus in any part of the body is a possible source of tuberculous meningitis.

SYPHILITIC DISEASE frequently attacks the membranes of the brain, either directly or by extension from disease of the bones of the cranium. The **dura-mater** is most commonly involved, and, in this membrane, the disease manifests itself either as a **meningitis, or as an arteritis,** or in the form of **gummata.**

1. **Meningitis** may affect the dura at any part, and give rise to wide-spread thickening of the membrane. The thickened area, which is fibro-cellular in its character, gradually grows by extension inwards, and, eventually, dura and pia become adherent. At the base, these changes sometimes cause compression of the nerves and vessels, especially where they enter or leave the various foramina, which have become narrowed by the thickening of the dura lining them. Optic neuritis, paralysis of the third, of the sixth, and, more rarely, of other, cranial nerves, headache, vertigo, etc., may be present as a result of the infiltration and com-pression of the various nerves, vessels, etc., by the newly-formed tissue.

2. **Arteritis.**—Endarteritis or periarteritis may occur, especially in the basilar artery and its branches. The middle cerebral is sometimes affected, and a wide-spread change, affecting many of the smaller arteries is frequently seen. The large vessels show mainly the condition of end-arteritis deformans (atheroma) : the smaller ones, endarteritis proliferans and periarteritis. In rare instances, there is development of discrete nodules along the arteries (nodose periarteritis [1]) or even along the veins.

3. **Gummata** may develop in the dura at any point, but are commonest towards the vertex. They, too, press upon, and infiltrate, nerves and vessels, and, by pressure on, and invasion of, the cranial bones, cause erosion, or even extensive necrosis.

The **pia-mater** may be affected by direct extension from syphilis of

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[1] Alexander Bruce, " Nodose Periarteritis," *Transactions of Edinburgh Medico-Chirurgical Society*, 1893, vol. xiii., p. 190; and Carnegie Dickson, " Polyarteritis Acuta Nodosa and Periarteritis Nodosa," *Jour. Path. and Bact.*, London, 1907, vol. xii., p. 31.

the dura, the lesion presenting itself as a **diffuse meningitis or as an arteritis. Primary syphilitic meningitis, arteritis,** and **gummatous formation,** sometimes in the form of miliary gummata, are found in the pia. The cerebro-spinal fluid shews generally a lymphocytosis and an increase in protein, and may give a positive Wassermann reaction.

TUMOURS OF THE MENINGES :—

Fibromas, Chondromas, Angiomas, Psammomas, Osteomas, Lipomas, Sarcomas, and **Endotheliomas** or **Mesotheliomas,** are described.

The endo- or meso-theliomas most commonly arise in the pia-mater, and may sometimes be associated with endotheliomas of bone. The sarcomas, especially those of the dura-mater, are probably the most important tumours of the meninges. They are situated generally at the base of the skull, and they extend and involve neighbouring parts—the pons, the medulla, the cranial nerves, the bones, etc. They are usually very malignant.

Teratomas occasionally occur. **Meningoceles** are described on p. 965.

CEREBRO-SPINAL FLUID [1]:—

Under normal conditions, the cerebro-spinal fluid is clear and watery, and of low specific gravity (1·004 to 1·007); it contains soluble inorganic salts, a trace of coagulable protein, which is chiefly globulin, and 0·05–0·13 of a copper-reducing substance that is probably glucose. It is practically free from cells or other formed elements. According to Halliburton, this fluid is a secretion arising from a definite glandular structure, and is produced primarily by secreting cells covering the choroid plexuses in the lateral ventricles. The pressure, therefore, is dependent to a considerable extent on the activity or secretory power of the secreting cells, though one cannot doubt that it is also influenced by changes in the arterial and venous pressures.

Under various abnormal conditions, the protein matter—albumin, globulin, or both of these—is largely increased, the cellular elements become a marked feature (*see under* **Meningitis, Syphilis, etc.**), and various abnormal substances such as cholesterol, etc., are added. The colour may be altered, from the presence of blood, blood-pigment, or other abnormal pigmentary substances.

ACCUMULATIONS OF CEREBRO-SPINAL FLUID IN THE MEMBRANES AND CAVITIES OF THE BRAIN :—

Œdema.—Marked œdema of the membranes of the brain, especially the pia-arachnoid, occurs, along with œdema in other parts, in some cases of Bright's disease, heart-disease, etc. It is by no means infrequent, in cases which have clinically exhibited symptoms—especially if supervening during the course of Bright's disease—suggesting some localised cerebral lesion such as hæmorrhage, thrombosis, or tumour, to find only

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[1] For a fuller description of the characters of the cerebro-spinal fluid in health and disease, *see* Chapter I., Buzzard and Greenfield's *The Pathology of the Nervous System*, Messrs. Constable, London, 1921.

marked general œdema of the membranes and brain-substance. In certain cases in which atrophy of the brain has taken place, the sub-arachnoid space may become filled with serous fluid (*see* p. 966); and definite local accumulations due to inflammatory changes—and described as **meningitis serosa circumscripta**—occur. This condition may arise in the course of infectious diseases or intoxications, or in some cases, apparently independently of these factors.

Hydrocephalus.—The commonest manifestation of this condition is that in which there is an excess of fluid in the whole ventricular system, but especially in the lateral ventricles. In certain congenital cases the
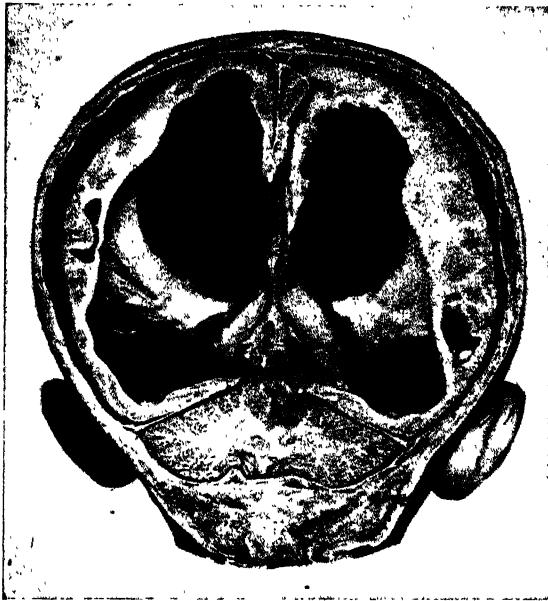
Fig. 430.—Coronal section through the Cranium and Brain of a case of Chronic Hydro-cephalus, shewing extreme distension of the Lateral Ventricles. (From the Patho-logical Museum, University of Sheffield.)

fluid accumulates in the subdural space (**External Hydrocephalus**), but these cases are so rare that further reference need not be made to them.

The **accumulation of fluid in the ventricles** may be **congenital** or **acquired.**

(*a*) **Congenital Hydrocephalus.**—In this condition, there is a gradual dilatation, especially of the lateral ventricles, with very marked thinning of the brain-substance and of the bones of the skull. The skull becomes greatly expanded, closure of the sutures is prevented, and the cranium may be represented by a membranous structure in which widely separated plates of bone are embedded. The frontal bone is pushed forwards so that the forehead rises perpendicularly or overhangs the eyebrows, the parietal bones bulge laterally, and the occipital bone is pushed backwards.

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In spite of the great thinning of the brain-substance and the pressure exerted on it, its functions may be retained. Usually, however, the hydrocephalic child gives evidence of varying degrees of mental enfeeblement. The lateral ventricles, as has been said, undergo the greatest degree of dilatation, but the foramina of Monro, the third, and even the fourth, ventricles may also be dilated. The lining-membrane of the ventricles is usually thickened, and may appear somewhat granular. The accumulated fluid is clear, watery, and of low specific gravity.

The **cause** of chronic hydrocephalus, in many cases, is obscure, but it is generally believed to be due to some congenital defect in the apparatus
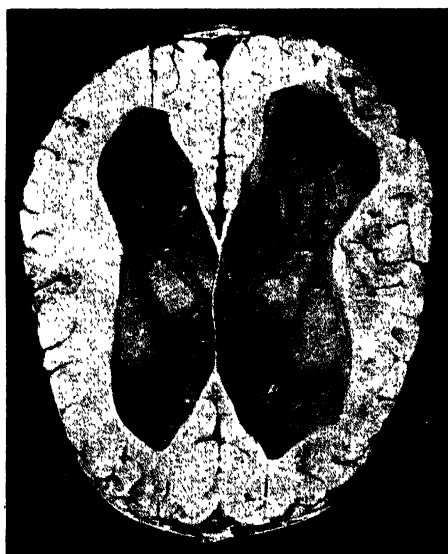

FIG. 431.—Horizontal section through the Brain of a case of Chronic Hydrocephalus, shewing the dilatation of the Lateral Ventricles and of the Foramina of Monro. (From a specimen belonging to Sir Harold J. Stiles, F.R.C.S.E.)

for the secretion and absorption of cerebro-spinal fluid, e.g. a mal-development and closure of the foramen of Magendie and the other foramina in the roof of the fourth ventricle. It must be recognised that, both in the **congenital** and in the **acquired** form of the disease, there may have been a primary slight attack of meningitis, either occurring in utero, or which had escaped observation at a later period.

(b) **Acquired Hydrocephalus.**—A simple basal or other form of meningitis may cause the scaling up of the foramina in the roof of the fourth ventricle, and so lead to the production of **Acquired Hydrocephalus.** This may supervene during the active stage of the disease, when it is undoubtedly aided by inflammatory reaction (transudation of lymph, etc.) which involves the choroid plexuses and the lining membrane of the ventricles; or it may occur during convalescence. A subsidiary, but important, phenomenon, aiding in the production of hydrocephalus, is

the impaction of the medulla and neighbouring portions of the cerebellum into the foramen magnum, due to increase in bulk of the cranial contents from congestion or œdema. Hydrocephalus itself, when once started, has a similar result, the two conditions, hydrocephalus and impaction, mutually aggravating each other. Some cases of acute hydrocephalus may be thus produced without actual closure of the foramina in the pial roof of the fourth ventricle by inflammation, and may occur during the active disease (in which case, and especially in meningococcal mening-itis, the causal organisms may be present in the ventricular fluid); or the hydrocephalus may supervene during convalescence.
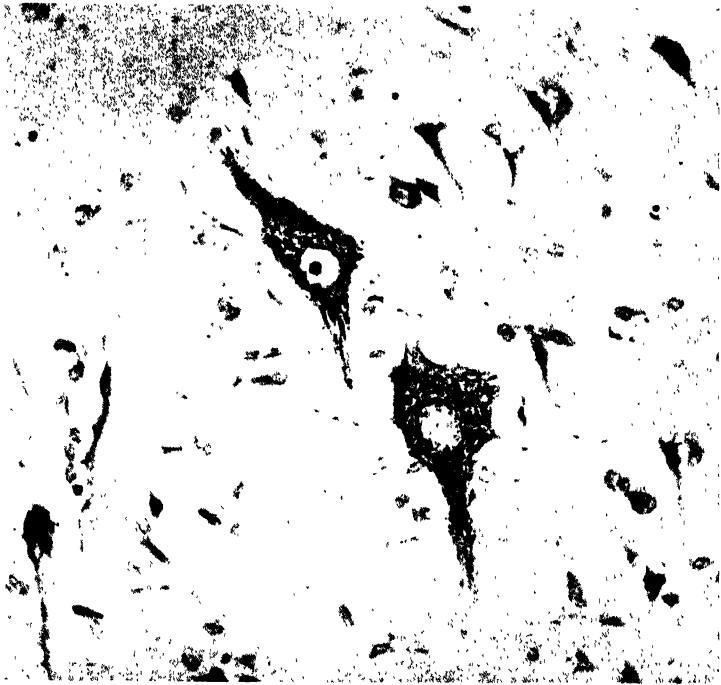
Fig. 432.—*Healthy Betz-cells*. Shewing nucleus and nucleolus (one cell), cell-processes and Nissl-bodies. (From specimen lent by Drs. Watson and Bigland, Liverpool.) × 300.

II. DISEASES OF THE BRAIN

In dealing with the diseases of the brain and spinal cord, there are certain elementary facts which require to be borne in mind. In general terms, the brain-tissue consists of the nervous tissue proper, the supporting tissue, and blood-vessels. Blood-vessels are very lavishly supplied. The main arterial trunks (vertebral and internal carotid), on entering the skull, are almost immediately resolved into an anastomosing circle (the circle of Willis). The internal carotid artery, after perforating the dura-mater, divides into the **anterior** and the **middle cerebral** arteries.

Just as the internal carotid artery passes through the dura-mater, it gives off the **ophthalmic artery,** and, from the latter, the **arteria centralis retinæ** arises. The **middle cerebral** artery supplies the third frontal, the

upper and middle temporal, the angular, the supra-marginal, and the lower two-thirds of the ascending frontal and parietal gyri, the anterior end of the temporal lobe, and, sometimes, the superior half of the inferior temporal gyrus. The anterior cerebral artery supplies the upper third of the ascending frontal and parietal gyri, the superior frontal gyrus, the corpus callosum and the mesial surface of the gyrus fornicatus, marginal gyrus, and the anterior three-fourths of the quadrate lobe. The occipital lobe, the temporo-sphenoidal convolutions, and various parts of the optic

FIG. 433.—*Degenerated Nerve-cells.* From the anterior horn of the spinal cord in a case of Pellagra, shewing eccentric position of nucleus, disappearance of Nissl-bodies, loss of processes, etc. (Lent by Drs. Watson and Bigland, Liverpool.) ×300.

thalamus, are supplied by the posterior cerebral artery. Of the **middle cerebral artery,** the most important branches are those supplying the basal ganglia, viz.—the **caudate,** passing to the head of the caudate nucleus : the **antero-lateral,** supplying the caudate nucleus—except its head—the internal capsule, and part of the optic thalamus : and the **lenticulo-striate,** supplying the lenticular nucleus and external capsule, and passing through the internal capsule into the caudate nucleus.

The two vertebral arteries, after giving off several branches, including the posterior meningeal and the posterior inferior cerebellar, join to form the **basilar** artery, and this, in its turn, gives off the other cerebellar arteries

and the posterior cerebral, which supply the cerebellum, the pons and the medulla.

Of the **veins,** the most important are those which leave the temporal and occipital lobes to end in the lateral sinus.

The nervous tissue is composed of **nerve-cells,** each of which consists of a cell-body and its nucleus. This cell is continued into an **axis-cylinder** process with its terminal arborisations and, usually, also many protoplasmic processes or **dendrites.** The supporting tissue consists of an epiblastic structure— neuroglia-cells and their fibres —in addition to ordinary mesoblastic connective tissue, the latter being found especially around the blood-vessels.

In degenerations of nervous tissue, from whatever cause, the nerve-cells and the nerve-fibres suffer most severely; and the neuroglia proliferates in order to replace the dead or damaged nerve-cells. The mesoblastic connective tissue plays very little part in the process.

CONGENITAL ABNORMALITIES.—MALFORMATIONS are seen principally in imperfectly developed fœtuses which do not survive birth, and are interesting rather from an anatomical, than from a pathological, point of view. The brain may be wholly or partially deficient (**anencephalia**), and this may be associated with absence of the whole or part of the cranial vault (**acrania** or **hemicrania**), and imperfect closure of the skull along the middle line (**cranioschisis**). In conjunction with imperfect development of the skull, hernia of the brain (**encephalocele**) or hernia of the membranes (**meningocele**) may occur. The meningocele consists merely of a protrusion of part of the cerebral membranes. In an encephalocele, there is, in addition, protrusion of part of the brain. These protrusions are generally found in the middle line posteriorly, between the two lateral halves of the occipital bone, *i. e.* in the occipital fontanelle of Sutton—a gap running up in the middle line from the inferior angle at the foramen magnum to the occipital protuberance : in the fronto-nasal suture : and, more rarely, in the lambdoidal, sagittal, and other sutures. They have been described as occurring through normal and abnormal fissures, at the base of the skull and into the orbit, nose and mouth. Associated with deficiency of the anterior part of the fore-brain, a single central eye (**cyclopia**) is sometimes found. In adult life, **general smallness of the brain (micrencephalus)** with corresponding smallness of the head (**microcephalus**) may be present. The term **Microcephaly** is applied generally, though not correctly, to smallness of the brain. The condition is characterised by an imperfect development of the gyri and sulci, these often being small, irregular in arrangement, and imperfectly formed. In certain cases it is due simply to defective development, but sometimes it results from definite pathological conditions in the fœtus. Thickenings of the pia-mater, suggesting early inflammatory conditions, have been found associated with it.

Parts of the brain are sometimes congenitally small in size. At certain areas in the cortex, the convolutions may be imperfectly formed. The hemispheres may be asymmetrical, or the cerebellum small and imperfect. The corpus callosum is sometimes absent.

"**HYPERTROPHY**," or, more correctly, **INCREASE IN THE SIZE, OF THE BRAIN,** may occur, without any apparent pathological alteration in the brain-substance. In other cases, however, this "hypertrophy" is associated with a hyperplasia of the neuroglial tissue.

ATROPHY OF THE BRAIN.—In general cachectic diseases, the brain does not waste to the same extent, or in the same proportion, as other body-structures; but, in old people, and especially in alcoholics, atrophy of the convolutions takes place. A similar condition is seen in general·paralysis of the insane, especially in the frontal region, and also in cases where arterial degeneration is a marked feature. The fluid in the meshes of the pia is increased, and the increase is sometimes mistaken for dropsy. There is no marked—though there may sometimes be slight—dilatation of the lateral ventricles. The pia is usually thickened and more adherent to the brain-substance than in the normal condition, and this thickening may be unilateral, or may appear as a general, or as a patchy, milky opacity, or in the form of irregular whitish nodules. The cranial bones usually become thinned, and may sink in slightly as the brain shrinks. The perivascular lymphatics may be dilated because of the atrophy and retraction of the surrounding brain-substance.

Local atrophy may result from the pressure of tumours, etc.: or from loss of functional activity, following hæmorrhage, embolism, or thrombosis, with subsequent softening and absorption. In such cases, cavities or pseudocysts, with a smooth lining and clear watery contents, may be formed; and there may also be an abnormal distension of the perivascular lymphatic spaces, owing to an accumulation of fluid in them, and to shrinking of the cerebral substance.

Injuries.—These owe their importance to the effects they have on the functions of the brain. The force of the blow causes disturbances of the circulation in, and of the structure of, the cerebral tissue. There may, in some cases, be no injury to the skull, but the **concussion,** such, for example, as that resulting from the bursting of an explosive shell, may produce various nervous symptoms (**shell-shock**), and, on *post-mortem* examination, evidence of punctiform hæmorrhages at the termination of the smaller vessels on the surface of the brain and in the grey matter elsewhere, or, in other instances, larger hæmorrhages, is found. The cerebro-spinal fluid may be blood-stained. Mott says there is a general chromatolytic change in the cells of the central nervous system—the cells most affected being the small cells in which the basophile substance has partly or almost wholly disappeared. In the larger cells, the Nissl-granules are small and not packed so closely together as in normal tissues.

Similarly, there may be **contusion** and **laceration** of the brain, with or without a wound of the skull. Bullet-·or shrapnel-wounds and fractures produce varying degrees of hæmorrhage and destruction of brain-tissue; and the pathological effects will depend on the site and extent of the

injury and the character of the missile, *e. g.* whether it is septic or not. Clean wounds of brain-tissue heal rapidly, whereas septic wounds may produce considerable areas of suppuration. Wounds deep into the brain may, after a relatively long period, be followed by encephalitis, abscess-formation, or meningitis. Von Eiselberg states that late abscess-formation, secondary to penetrating wounds of the skull, may not infrequently supervene, if the cases subsequently become the subject of slight traumata, infectious disease, or even a sore throat.

CIRCULATORY DISTURBANCES :—

1. **CHRONIC VENOUS CONGESTION,** as a *post-mortem* phenomenon at all events, is not usually marked in the brain. Even in cases of mitral disease, with extensive venous congestion in the lungs, liver, etc., the only evidence of the condition in the brain may be distension and tortuosity of the vessels in the pia-mater, and a slight deposit of pigment round these vessels. The condition may result from thrombosis of the sinuses, but, even in such cases, the appearances visible after death are insignificant.

2. **ŒDEMA or DROPSY** of the brain-substance is not common except in cases of Bright's disease, though it occurs to a varying extent in acute inflammation of the brain-substance, or of the pia-arachnoid. The brain is usually firmer than normal, and, when cut across, presents a glistening, watery appearance, the fluid in the ventricles being also increased in amount, and the meshes of the pia-arachnoid containing excess of fluid. As already mentioned, these may be the only naked-eye lesions in certain cases, especially of Bright's disease, where the clinical symptoms (*e.g.* monoplegia, hemiplegia, etc.) may have suggested some more definitely localised cerebral lesion such as hæmorrhage or embolism.

Local œdema may be present in the neighbourhood of tumours, hæmorrhages, etc.

3. **ANÆMIA.**—Apart from the transitory anæmia of cardiac syncope, general anæmia of the brain results from loss of blood, from stenosis of the aortic orifice, from general loss of fluid, as in prolonged diarrhœa, etc., and in blood-diseases where there is extensive destruction of the red blood-corpuscles. Though such anæmia may be a cause of death, there are no characteristic *post-mortem* appearances in the brain.

Local anæmia (Ischæmia) may arise from local pressure on the brain, produced by tumours, extravasations of blood, inflammatory exudates, etc.; but the commonest and most important cause is obstruction of arteries.

4. **ARTERIAL OBSTRUCTION** may be produced by embolism or by thrombosis. The **embolus** is usually a portion of a vegetation detached from the mitral or the aortic valve, or a portion of a thrombus or clot situated in one of the left chambers of the heart, on an atheromatous patch in an artery, or in an aneurism of the aorta. Partial obstruction,

and even temporary complete obstruction, without thrombosis, caused by irregular spasmodic contraction of the muscular coat of the vessel is said to occur in arteries whose lumen is greatly narrowed by degenerative and proliferative changes in their walls.

Thrombosis from causes other than embolism is less frequent, and is usually secondary to atheroma or other degenerative condition of the arteries, though, in very exceptional cases, it may be due to a general enfeeblement of the circulation, or to disease of the blood.
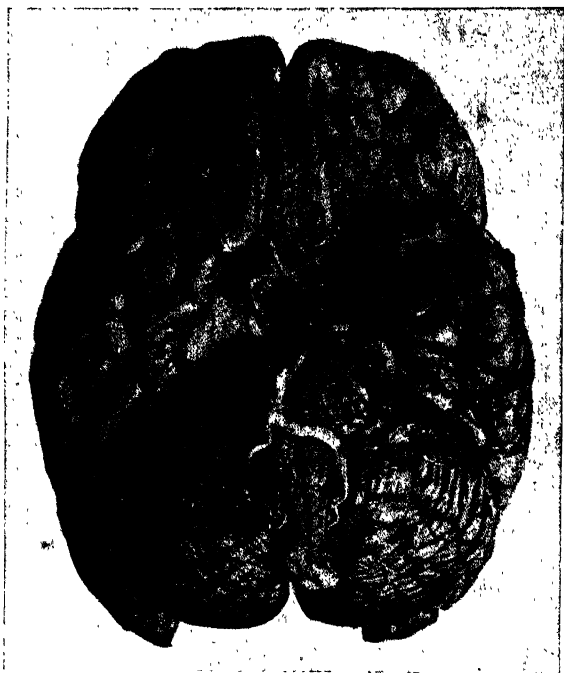
Fig. 434.—Atheroma of the Vessels at the base of the Brain, shewing tortuosity and irregular dilatation. The Carotids and Vertebrals on each side shew great inequality in size.

Regions specially liable to be affected by arterial obstruction :—

(a) **Embolism** usually occurs in the left middle cerebral artery and its branches, on account of the direct continuity of this vessel with the corresponding internal carotid—the artery, which, owing to the anatomical arrangement of the vessels, provides the most direct course for an embolus. Next, in order of liability, come the right middle cerebral and the posterior cerebral (in the case of the latter, the two sides being equally liable), the vertebral—the left more commonly than the right—the anterior cerebral, the cerebellar, especially the posterior inferior cerebellar, and the basilar, the last three, however, being only rarely the seat of emboli.

(b) **Thrombosis, as a result of atheroma,** is found especially in branches

of the posterior cerebral and the basilar arteries, or in some of the smaller cortical branches. As a result of **proliferative endarteritis,** the thrombosis occurs particularly in the internal carotid and middle cerebral, and also in the basilar, the posterior cerebral, and the vertebral arteries.

Pathological Anatomy.—The **effects of the obstruction,** however produced, will depend on its situation, its extent, the condition of the arteries affected, and the amount of collateral supply that is possible. Thus, obstruction of the **middle cerebral artery** will cut off the supply from the motor and sensory areas in the basal ganglia, and will produce hemiplegia with, possibly, aphasia, etc., thus giving definite clinical manifestations for localisation of the lesion; or thrombosis of the **basilar artery,** causing softening in the pons, may give rise to bilateral hemiplegia. Again, if the obstruction take place in a main artery, or in one of its minute branches, the pathological effects may be very severe, or very slight, according to the importance and extent of the area of brain-tissue involved, and the amount of collateral supply available; or, if the obstructing body become broken up into fragments, these will be distributed, causing multiple localised areas of damage. More important, however, are the site of the vessels, and the condition of their walls. If the collateral supply is deficient, or if widespread disease of the arteries prevents its full establishment, the pathological results of obstruction are more serious. The nutrient arteries supplying the brain-tissue do not anastomose freely with one another, and occlusion of them has very serious results; whereas obstruction in some vessels in the circle of Willis, where the anastomosis is well marked, may lead to only a temporary derangement of the circulation. The situations in which softening will occur can be determined only by a careful anatomical study of the arteries of the brain and their distribution-areas.

Phenomena observed as a result of obstruction:—

Within a few hours after the obstruction, in cases which do not succumb to its immediate effects, there is hyperæmia in the pia-mater—if the lesion be cortical—and in those parts of the brain bordering on the region from which the arterial supply has been cut off. This hyperæmia, especially of the cerebral substance, very soon passes off, and the parts supplied by the obstructed artery speedily become pale and soft. Gradually, this softening becomes more marked, and the affected part is converted into a mass of creamy pulp. If small and superficial, the softened area may be absorbed and leave a depression on the surface of the brain. If in the interior of the brain, partial absorption takes place, and a cavity, containing somewhat turbid fluid, generally remains. Usually, this cavity has no distinct cyst-wall, and there is, as a rule, no deposit of pigment, such as is seen after hæmorrhage. Unless secondary extension takes place, the softened area is always smaller than the area supplied by the obstructed artery.

On microscopical examination, the nerve-fibres are found to be

disintegrated, the myelin becoming fragmented and escaping from the nerve-sheath. The nerve-cells are somewhat more resistant than the fibres, but they also become granular, and eventually disappear. The cells of the neuroglia, and those lining the vessels, undergo fatty degeneration, forming the so-called " compound granular corpuscles." Hæmorrhage may be present, in some cases, in varying amount, but, gradually, the hæmoglobin dissolves out from the red cells and is diffused throughout the tissues. Thus, the red colour of these softenings with hæmorrhages (red softening) gradually changes to yellow (yellow softening) and eventually to white (white softening).

CEREBRAL HÆMORRHAGE.—Under this term are generally included two conditions—hæmorrhage in, or upon the surface of, the membranes of the brain—best termed meningeal hæmorrhage, and hæmorrhage into the substance of the brain. To the latter, the term cerebral hæmorrhage, in its strict sense, should be confined.

Extra- and intra-dural hæmorrhages have already been dealt with. Subdural hæmorrhages, or hæmorrhages internal to the dura-mater, are due to bleeding either from without, or from laceration of some vessel in or on the surface of the cortex, e. g. the rupture of an aneurism. They are, however, generally the result of traumatism, though rupture of vessels may take place during a violent spasm in whooping cough, or during a convulsive seizure.

Sub-arachnoid hæmorrhages are more important, and may extend over a considerable surface of the brain, the blood being confined to the sub-arachnoid space and the meshes of the pia. Such hæmorrhages may be the result of injury to the brain from a blow or a fall, the brain-substance being lacerated, but the membranes not necessarily being torn; or they may follow thrombosis of the longitudinal sinus, where the smaller tributary vessels become dilated and undergo rupture.

Small hæmorrhages may occur as a result of severe inflammation, or in toxic diseases of various kinds, e.g. septicæmia, scurvy, typhoid fever, pneumonia, measles, etc., and punctiform hæmorrhages are very common in gas-poisoning; whilst in anthrax, as has been mentioned on p. 951, and in cerebro-spinal fever, hæmorrhages of considerable size are found both in the substance and in the membranes. Blood under the pia-arachnoid may be associated with the rupture of a small aneurism on a pial vessel, or an extension from the rupture of a larger aneurism on the vessels at the base of the brain. Commonly, blood under the pia-arachnoid, especially at the base of the brain, has spread from a hæmorrhage which has burst into the lateral ventricles. The blood makes its way through the foramen of Monro into the third ventricle, and then passes along the aqueduct of Sylvius into the fourth ventricle, from which it escapes into the sub-arachnoid space, where it may burrow, covering both the under and the upper surface of the cerebellum, and perhaps also extending to the cerebrum, and spreading along the lines of the fissures of Sylvius, or passing anteriorly into the longitudinal fissure,

over the upper surface of the corpus callosum, and into the sulci on the inner surface of the hemispheres. It may also extend down the cord and be found on lumbar puncture.

Cerebral Hæmorrhage, properly so-called, is due generally to rupture of some of the blood-vessels within the substance of the brain. The arteries usually shew atheroma of their walls, and, in a certain proportion of cases, aneurismal dilatation—the aneurisms varying in size, some being single and measuring perhaps three-quarters of an inch to an inch in diameter, others being microscopic in size and perhaps multiple (**miliary aneurisms**). Rupture of either of these varieties may produce extensive

Fig. 435.—A minute (miliary) Aneurism on one of the Cerebral Arteries. ×.75.

cerebral hæmorrhage. The **larger aneurisms** are developed on any artery, being seen especially on the vessels of the circle of Willis, on the vertebral artery, on some of the internal branches of the middle cerebral, and, less commonly, on the basilar, internal carotid, posterior cerebral, anterior communicating, and cerebellar. The **miliary aneurisms** are commoner on the arterial branches which supply the basal ganglia. Both forms result, as a rule, from degenerative changes in the walls of the arteries, associated with increased pressure within the vessels—these conditions being present especially in certain types of Bright's disease, particularly when accompanied by hypertrophy of the left ventricle, the forcible action of which, along with the high intravascular pressure and weakening of the vessel-wall, may lead to rupture of the aneurisms.

Such aneurisms may, in certain parts of the brain (especially in the medulla), and also in the spinal cord, give rise to serious pressure-

symptoms, and may even, quite apart from rupture, lead to a fatal issue. In children, the aneurismal dilatations, which by their rupture lead to cerebral hæmorrhage, appear to be due commonly to some congenital defect in the vessel-wall, especially in its muscular coat.

Cerebral hæmorrhage frequently occurs in acute fevers, *e.g.* cerebro-spinal fever, in septicæmia, in pernicious and other forms of anæmia, in leucocythæmia, and in phosphorus-poisoning. In all these cases, the important factor is degeneration of the walls of the smaller vessels, and the hæmorrhages may be small and widely-scattered, or of considerable
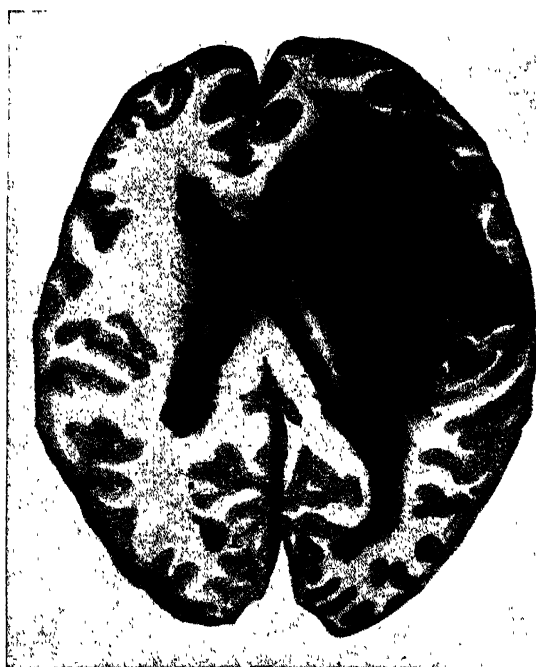
Fig. 436.—Large Cerebral Hæmorrhage in the region of the Basal Ganglia, which has burst into the Lateral Ventricle.

size, as in leucocythæmia, in which disease the effusion may be a large, localised one, which may destroy the brain-tissue very extensively.

Sites of Cerebral Hæmorrhage.—The commoner situations in which hæmorrhage takes place are, according to Greenfield, in order of importance, as follows :—

1. In the vicinity of the **basal ganglia** (75 per cent.), at the upper part of the external capsule : also towards the upper and outer part of the lenticular nucleus : or in the adjoining part of the internal capsule—from any of which points it may spread and involve the centrum ovale, or destroy the basal ganglia and burst into the lateral ventricles.

2. In **the pons** (10–12 per cent.), where also pigmented areas, representing the situations in which hæmorrhage had previously taken place, are often seen in cases of **Bright's disease** or in **general arterio-sclerosis.**

3. In the **meninges** (12 per cent.—already considered).

4. In the **cerebellum** (1 per cent. or less).

Ventricular hæmorrhage is almost invariably **secondary** to hæmorrhage into the substance of the brain, and originates from the smaller branches of the anterior and the posterior cerebral arteries—the former at the tip of the caudate nucleus, the latter at the posterior end of the optic thalamus—or from the middle cerebral, the blood ploughing its way through the lenticular nucleus. Gowers states that it may occur as a result of rupture of an aneurism on the choroid plexus.

The characters of the hæmorrhage.—The amount of the hæmorrhage depends, to a certain extent, on the size of the ruptured vessel and on the nature of its support and surroundings. If rupture takes place into the white matter of the centrum ovale, the blood tends to spread very widely, whereas, in the case of rupture into the internal capsule, the spread may be less extensive. The brain-tissue is ploughed up and contused, and, as evidence of contusion, numerous minute punctate hæmorrhages are seen in the softened brain-tissue around the larger hæmorrhage. There may be some œdema following the hæmorrhage, and this may increase the area of damage to the brain-tissue. A **series** of hæmorrhages may occur at different times, either from the same vessel or from vessels around the primary hæmorrhagic area. These hæmorrhages sometimes coalesce and produce more or less extensive destruction of the brain-tissue.

If the hæmorrhage does not prove fatal, **partial absorption** takes place. The hæmoglobin is freed from the red cells, part of it is transformed into hæmosiderin and part is deposited as hæmatoidin crystals. Granulation-tissue is formed—the connective-tissue, however, is usually scanty. The surrounding neuroglial tissue also proliferates to a limited extent, and, finally, there is produced a pseudocyst filled with fluid, and having for its wall the proliferated connective and neuroglial tissue. Some contraction of the brain-tissue in the neighbourhood usually follows. Acute inflammatory softening may occur round the old hæmorrhage.

Hæmorrhage from the middle cerebral artery.—Of the branches of the middle cerebral artery which pass through the anterior perforated space, some are given off directly into the substance of the lenticular nucleus. One, the **lenticulo-striate** (fig. 437, 4), passes between the lenticular nucleus and the claustrum, and enters the caudate nucleus. Rupture of the latter vessel is of such frequent occurrence that it has been termed " **the artery of cerebral hæmorrhage.**" The starting-point of the hæmorrhage from this vessel is very frequently in the external capsule or the outer part of the lenticular nucleus, the blood ploughing its way into the lenticular nucleus, and reaching even as far as the lateral ventricles. If the hæmorrhage in these situations is near the anterior end of the nucleus, it

may spread into the centrum ovale. Hæmorrhage in the region of the claustrum is not uncommon, and forms a barrier, often linear in outline, separating the lenticular nucleus from the island of Reil. Hæmorrhage into the internal capsule is sometimes secondary to these more external hæmorrhages, though rupture of the lenticulo-striate branch may involve primarily the motor part of the capsule, *i. e.* the genu and the anterior
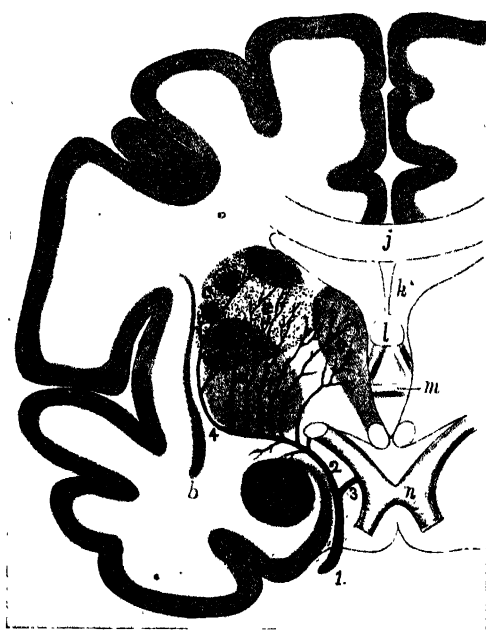

Fig. 437.—Diagrammatic View of the Basal Ganglia and their Blood-Supply, seen in coronal section.

a, Island of Reil. *b*, Claustrum. *c*, External Capsule. *d*, Nucleus Lenticularis. *e*, Internal Capsule. *f*, Nucleus Caudatus. *g*, Optic Thalamus. *h*, Nucleus Amygdalæ. *j*, Corpus Callosum. *k*, Lateral Ventricle. *l*, Fornix. *m*, Anterior Commissure. *n*, Optic Chiasma.
1. Internal Carotid Artery. 2. Middle Cerebral Artery. 3. Posterior Cerebral Artery. 4. Lenticulo-striate Artery. The "dotted" part represents the area in which hæmorrhage usually occurs—the three darker spots in this area representing the common sites of origin of the hæmorrhage.

two-thirds of the posterior limb; whilst hæmorrhage from the lenticulo-optic branch may spread to, and destroy, the sensory fibres in the posterior third of the posterior limb of the capsule.

Hæmorrhage from the anterior cerebral artery.—The branches of this artery which especially give rise to cerebral hæmorrhage are those which supply the anterior part of the caudate nucleus, more particularly the part projecting into the lateral ventricles. Thus, this artery is the commonest source of **ventricular hæmorrhage,** which, however, also results from rupture of the branch of the **posterior cerebral artery** which supplies the optic thalamus.
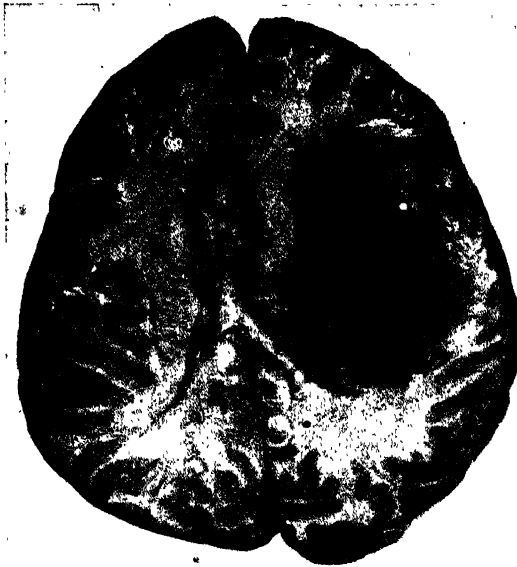
Fig. 438.—Large Cerebral Hæmorrhage into the Region of the Internal Capsule and Basal Ganglia.

Fig. 439.—Hæmorrhage at the posterior part of the Lenticular Nucleus and Internal Capsule with Rupture into both Lateral Ventricles.

Hæmorrhage into the pons comes next in frequency to hæmorrhage into the basal ganglia. The hæmorrhage may be large, and may destroy a considerable portion of the substance of the pons. Minute hæmorrhages are, however, of commoner occurrence.

Fig. 440.—Hæmorrhage into the Pons.

Hæmorrhage into the cerebellum is extremely rare.
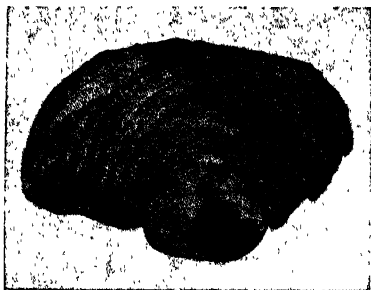
Effects of Hæmorrhage.—Large hæmorrhages are usually fatal; but, if the hæmorrhage is small, and no vital centre is involved, recovery may take place. A pigmented area, in some cases with the formation of a small cavity, possessing a definite wall, —the result of connective-tissue and neuroglial-tissue proliferation—may remain as the only sign of the previous hæmorrhage.

As a result of hæmorrhage with destruction of brain-substance, secondary degenerations supervene—their nature and localisation, and the cerebral and spinal nerve-tracts in which they occur, depending on the position and the extent of the hæmorrhage; but, as the study of these involves anatomical and physiological, rather than pathological, details we do not think it necessary to enter into the discussion of them.

INFLAMMATION OF THE BRAIN :—

(*a*) **ACUTE INFLAMMATION (ENCEPHALITIS),** as a primary condition, is rare. Though usually secondary to an acute inflammation of the membranes, or to a local reaction round clots, tumours, chronic abscesses, or injuries, a primary encephalitis has been described as occurring in cases of scarlet fever, measles, influenza, pneumonia, whooping cough, mumps, diphtheria, cerebro-spinal meningitis and other diseases of a similar nature. The tissue affected is, in the early stages, red and injected, owing to the dilatation of the small vessels. Minute hæmorrhages may be present, and there may be well-marked localised œdema. The inflammatory area soon becomes soft and diffluent, and assumes a yellowish colour. **On microscopical examination,** collections of polymorphonuclear leucocytes are seen, and destructive changes in the nerve-cells and fibres are present. These pathological conditions are, as a rule, found as irregular foci and not widely scattered throughout the brain.

Epidemic Encephalitis (Encephalitis Lethargica).—In this disease, in which the cardinal symptoms are **lethargy, general asthenia, muscular rigidity,** and **cranial nerve-palsies,** Marinesco states that there are, visible to the naked eye, disseminated punctiform hæmorrhages in the grey matter of the floor of the fourth ventricle, the aqueduct of Sylvius, and even in the third ventricle. They are found also in the posterior part of the pons and of the peduncles. In the pons, the medulla, the

peduncles, and in the first segment of the spinal cord, he describes four kinds of lesions.

(1) An infiltration of lymphocytes and plasma-cells in the adventitia of the small vessels, especially the veins.

(2) Foci of interstitial inflammation in which there is some proliferation of the neuroglial cells at the roots of the nerves,.e.g. hypoglossal, pneumogastric.

(3) Various lesions of the nerve-cells—gradual disintegration and disappearance of . the Nissl-bodies, fragmentation of the nucleus, (karyorrhexis and pyknosis), vacuolation of the cytoplasm, etc.
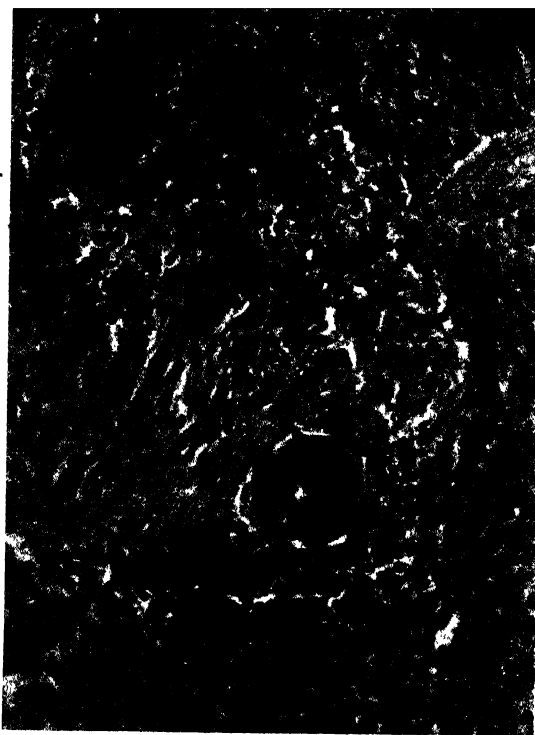
Fig. 441.—*Encephalitis Lethargica.* Section of brain shewing thrombosed vessels and hæmorrhage. (Lent by Dr. Watson, Rainhill Asylum, Liverpool.) × 100.

(4) Foci of hæmorrhage, to which reference has already. been made.

Mott regards this disease as an acute inflammation of the perivascular lymphatics, characterised by hæmorrhages in the pons, the medulla, the peduncles and around the third ventricle. In the lymphatic sheaths of the arteries and veins, in addition to lymphocytes and plasma-cells (figs. 442 and 443), there are large numbers of polymorphonuclear. leucocytes which are found in the tissues surrounding the vessels, as well

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as in the adventitia.   There is proliferation of the neuroglial cells around the vessels and in the adjacent nervous tissue.

Some cases have been described where the small-celled perivascular infiltration was present in the posterior horns of the cervical and lumbar cord.   No definite causal organism has been found, though some writers regard the condition as a polio-encephalitis, and the virus as analogous

Fig. 442.—*Cerebral Cortex.*   From a case of Encephalitis Lethargica of four weeks' duration, shewing perivascular infiltration with small round cells and also congestion (dark lines).   (Lent by Dr. J. G. Greenfield, National Hospital for Paralysis and Epilepsy.) × 50.

to, if not identical with, the virus of poliomyelitis.   Buzzard and J. G. Greenfield [1] state that—

" (1) Vascular congestion has been the most striking feature of all the cases examined within the first few weeks of the onset of symptoms. It affects all the vessels down to the smallest capillaries (fig. 442).

" (2) The changes in the nerve cells are extremely constant, but they are by no means universal.   Some of the nuclei of the brain stem may shew very little change when others close to them have many cells affected.   In general only a few of the nerve cells of a nucleus or area are affected, but all may shew some degree of alteration.   These changes, which have been well described by Marinesco, are perinuclear

[1] Buzzard and Greenfield, *Brain*, Vol. XLII., Part IV. 1919, pp. 305 *et seq.*

chromatolysis, eccentricity of the nucleus (figs. 433 and 455), excess of pigment, and, perhaps most constant of all, neuronophagy.[1]

" (3) It seemed clear that the cells taking part in this neuronophagy were, for the most part, derived from the mesoblastic elements, many being closely allied to plasma cells. They resembled in every respect the rows of round cells which could be seen in the same field lying

FIG. 443.—*Encephalitis Lethargica.* Shewing dilated vessels, areas of haemorrhage, and perivascular increase in cells. (Lent by Dr. Watson, Rainhill Asylum, Liverpool.) × 50.

along the outside of the capillary walls. Their cytoplasm is free from granules, and its outer border is rounded and clearly defined, and they occur at a stage of the disease when there is little evidence of glial proliferation. They were seen in large numbers among the nerve cells of the most affected nuclei, and to a less extent throughout all the nervous tissue. In some parts of the cortex, and in a few of the nuclei of the brain stem, almost every nerve cell had several such cells in close relation to it.

" In one or two of the cases which showed the greatest changes there

[1] Absorption of the nerve-elements by phagocytic cells.

are small collections of such cells in some parts of the pons and mid-brain. But dense clusters of cells such as those which invade the anterior horns of the cord in cases of poliomyelitis were never seen.

" (4) Round-celled perivascular infiltration (fig. 442) was present to a greater or less degree in all the cases examined within the first month or two of the onset of symptoms. But in two cases it was so inconspicuous

Fig. 444.—*Encephalitis Lethargica.* Shewing dilated and thrombosed vessel (the wall of the vessel has retracted from cortical tissue during preparation of section). (Lent by Dr. Watson, Rainhill Asylum, Liverpool.) × 50.

a feature that a careful search was necessary to find any vessel which shewed this change. It is not nearly so universal as is the infiltration of the tissues with plasma cells and lymphocytes, and is always patchy; either it picks out only a few vessels, or when the majority are affected they shew great variety in the thickness of the cuff of cells with which they are surrounded. These cells may obviously either be leaving the blood-vessel or returning to it. Several observations tend to support the theory that the majority of these cells are on their way back to the vessel.

" (5) In most of the cases there was some evidence of glial proliferation, but this formed a conspicuous feature in only one case. This patient died at the end of the sixth week of the disease and shewed the typical changes of the disease in an extreme degree. In the subcortical layers there was a great proliferation of neuroglial cells, shewing themselves as large irregular cells, with long fleshy processes, and one or. more oval nuclei lying near the margin of the cell."

Venous thrombosis with hæmorrhage (figs. 433 and 444), they state, were sufficiently common to deserve mention. A normal cerebro-spinal fluid is the rule, but, in some cases, an increase of lymphocytes has been found. Barker [1] reports an almost constant increase in the amount of sugar in 15 cases examined. The variations in the cerebro-spinal fluid are due possibly to the extent and the situation of the encephalitis.

Fig. 445.—*Cerebral Abscesses.* The lower one, in the temporo-sphenoidal lobe, was due to infection through the roof of the tympanic cavity and dura in a case of disease of the middle ear.

(b) **SUPPURATIVE INFLAMMATION (ABSCESS).**—Two forms of suppurative inflammation occur in the brain—one, due to the carriage of organisms to the brain by the blood-stream in cases of pyæmia, the other, due to local extension from inflammatory foci in the parts around.

1. **Pyæmic abscesses** are usually multiple, and may occur in any part of the brain. They are not common, but may be found more especially as a secondary complication of abscesses, or of suppuration in bronchiectatic or other cavities, in the lung, and in suppurative conditions of the pleura. Abscesses sometimes occur from septic embolism, in cases of ulcerative endocarditis.

2. **Abscesses due to direct extension.**—The most typical example of this condition is the abscess which follows suppurative disease of the middle ear. The infection may spread directly upwards, causing destructive changes in .

[1] L. C. Barker and Collaborators, *Amer. Jour. Med. Sc.*, Feb., March, 1920.

the bone and dura over the tympanic cavity, and the production of an abscess in the **temporo-sphenoidal lobe;** or it may spread backwards to the mastoid antrum and cells, producing septic phlebitis and thrombosis of the lateral sinus, and abscess-formation in the **cerebellum** or **cerebrum.** Occasionally, in middle-ear disease, abscesses develop in the above-mentioned positions, with no apparent naked-eye involvement of the dura or of the bone forming the roof of the tympanic cavity. In such cases, the infective material may be carried by lymphatics or possibly by small anastomising blood-vessels, especially minute veins.

Abscesses in the brain may also arise by direct spread from the bone or from the dura-mater —a subdural abscess being first formed; and this

Fig. 446.—*Section of the Medulla.* From a case of Insular Sclerosis, shewing Areas of Sclerosis (pale parts). (Pal-Weigert Method.) × 3.

involving the brain secondarily. Or, the septic material in the bone may spread by the veins or the venous sinuses, in the form of an infective thrombo-phlebitis. Injuries to the head, especially compound fractures, and diseases of the nose and orbit, are also not infrequent causes of the formation of cerebral abscesses.

Characters of the Abscesses.—In size, they vary considerably, and, in the more typical cases—those secondary to disease of the middle ear—the pus is usually greenish in colour, of a thick creamy consistence, and exhales a putrid odour. The abscess is commonly somewhat chronic, .is bounded by a distinct wall or "membrane" formed of granulation-tissue, generally enlarges gradually, and • sometimes bursts into the lateral ventricles or on the surface of the brain. •

Actinomycotic, and also rarer forms of Streptothricial, abscesses may occur.

(d) CHRONIC ENCEPHALITIS.—Under this term are described various forms of sclerosis of the brain, to which only brief reference need be made. Some of these are inflammatory in nature, whilst others are purely degenerative.

. (i) Disseminated or Insular Sclerosis.—The cause of this condition is unknown, but it has been found in association with some of the acute infective diseases, especially influenza, typhoid fever, smallpox, and scarlet fever. The causal connection of these diseases with it has not been clearly

Fig. 447.—*Thickening of the Pia-arachnoid.* From a case of General Paralysis of the Insane. (Lent by Drs. Watson and Bigland, Liverpool.) ; 50.

established and the condition certainly occurs independently of them. It is characterised by the occurrence of irregular patches of chronic inflammation or degeneration in the white matter beneath the cortex, in the centrum ovale, in the corpus callosum, in the grey matter of the basal ganglia, and in the pons, the medulla and the spinal cord (*see* figs. 446, 460, and 461). A more detailed account of the appearances will be found under Diseases of the Spinal Cord (*see* p. 1005). The irregular distribution of the sclerosed patches in the cord, medulla, pons, peduncles, cerebrum, and cerebellum, is the explanation of the very varied clinical manifestations of the disease. In Huntington's chorea, a form of sclerosis, the cortex of the anterior and middle regions of the brain is mainly involved.

(ii) **General Paralysis of the Insane.**—This disease is now regarded as a *late manifestation of syphilis*. *Spirochæte pallida* has been demonstrated in the lesions, and the Wassermann-reaction is usually positive with the cerebro-spinal fluid. During the **acute** period, the brain is swollen; and hyperæmia, and multiple foci of leucocytic infiltration and capillary hæmorrhages, are observed. In the **chronic** stage, there is thickening of the membranes, with degeneration and atrophy of brain-substance. The **pia-arachnoid** is frequently thickened and œdematous (figs. 447 and 448),

Fig. 448.—*General Paralysis of the Insane.* Section through a cortical sulcus, shewing thickening and congestion of the pia-arachnoid, and glial proliferation. (Lent by Drs. Watson and Bigland, Liverpool.) × 200.

the fluid in the meshes occurring mainly over the parietal and occipital lobes. The pia is adherent to the convolutions, which are irregularly atrophied. The **dura-mater** is very much thickened, and usually unduly adherent to the bones of the skull. **Chronic hæmorrhagic pachymeningitis** is very liable to occur (*see* p. 952). Arterio-sclerotic changes, especially in the basilar arteries, are noted.

On section, the brain is usually œdematous, and the lateral ventricles dilated. **On microscopical examination,** the nerve-cells are found to be especially affected. The nucleus and the granules disappear, and the cell-body undergoes atrophy. The myelin-sheath of the white fibres becomes more or less disintegrated, and a neuroglial proliferation (figs. 448, 449 and

450), with increase of the nuclei, takes place. The spider-cells are increased, and there is proliferation of the glial cells. The blood-vessels shcw thickening of their walls, the inner as well as the outer coat undergoing proliferation. The perivascular tissues are infiltrated with small lymphocyte-like, and plasma-, cells. All these changes are best seen in the cortex, but may also be found in the basal ganglia, pons, and medulla.

TUBERCULOSIS OF THE BRAIN—apart frbm tuberculous meningitis, already described on p. 957, and in which a certain degree of involve-
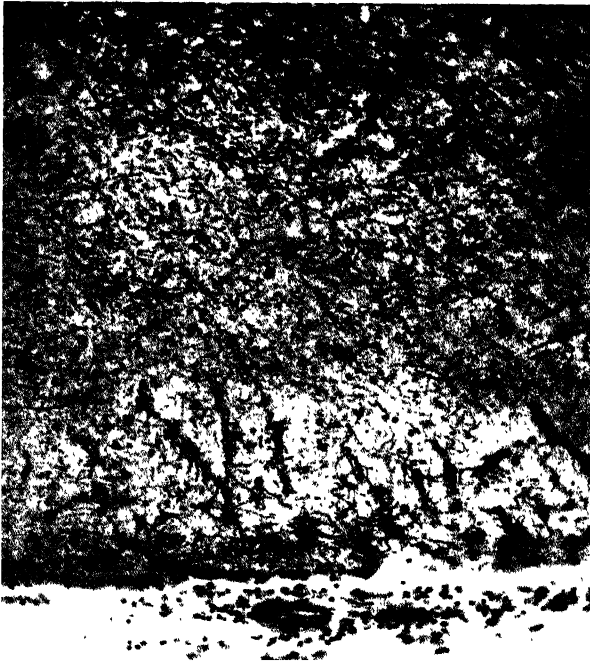

Fig. 449.—*General Paralysis of the Insane.* Outer layer of cerebral cortex, shewing marked glial proliferation. × 50. (Lent by Drs. Watson and Bigland, Liverpool.)

ment of the brain substance itself may supervene—occurs in the form of irregular **tumour-like nodules,** which are found in any part of the brain, but are commonest in the cerebellum. They are single or multiple, and vary much in size, sometimes reaching an inch or more in diameter. They occur especially in young people, and on **naked-eye examination,** are clearly outlined and shew a yellowish caseous centre. **On microscopical examination,** the nodule is composed of an amorphous caseous mass, with a peripheral zone of giant-celled tubercle-granulations, which gradually merge into the surrounding brain-substance. These tumours may reach the surface and give rise to tuberculous meningitis; or, by pressure on the straight sinus or on the veins of Galen, cause dilatation of the lateral

ventricles and **chronic hydrocephalus.** They may also lead to serious results by infiltrating or pressing upon important parts of the brain.

SYPHILIS OF THE BRAIN.—Syphilitic disease of the membranes (**meningitis, gummatous formation,** and **arteritis**) has been dealt with on p. 959. A gumma of the membranes sometimes extends into the substance of the brain, but **primary gummata** are found also in the brain-substance,

Fig. 450.—*Cerebral Cortex from a case of General Paralysis of the Insane.* Shewing proliferation of glia. × 300. (Lent by Drs. Watson and Bigland, Liverpool.)

e. g. in the corpus callosum, in the basal ganglia, in the pons, and the medulla. The walls of the vessels, in such cases, are generally thickened, and a **periarteritis** is common. This periarteritis is evidenced by the large number of mononucleated cells in and around the walls of the vessels. **Periarteritis nodosa** (p. 554) is a manifestation of syphilis and may occur in the brain. Small or **miliary gummata** may be scattered throughout the brain; but multiple patches undergoing sclerosis, and due to diffuse syphilitic granulation-tissue formation, are not common. The gummata may press upon, or infiltrate, the cranial and spinal

nerves; and the arterial degeneration may lead to thrombosis and softening of the brain.

Locomotor ataxia (p. 1007) and **General Paralysis of the Insane** (p. 984) are now generally regarded as a sequel of syphilis.

TUMOURS OF THE BRAIN.—The commonest tumours of the brain are gliomas and sarcomas. The **glioma** of the brain is usually an infiltrating tumour, and, **on section,** it is often difficult or impossible to make out any line of demarkation between the tumour and the brain-substance. **Hæmorrhage** into it is frequent. **On microscopical examination,** the tumour is composed of rounded or somewhat irregular cells, with or

•Fig. 451.—*Glioma of the Brain*•

without branching processes—the cells being embedded in a granular, homogeneous, or finely-fibrillated ground-substance, which sometimes is mucoid in character, and hence the designation of **myxoglioma.** Such tumours exhibit all degrees of malignancy. Some are comparatively simple, whilst others rapidly infiltrate the surrounding tissues, but metastases resulting from them are uncommon. Though these malignant forms are classified as malignant hylomata, they are practically identical in their characters with other forms of sarcoma. Gliomas also occur in the retina.

Sarcoma of the brain is usually of the round-celled type, and presents no special characters in this tissue as distinguished from sarcomas elsewhere.

Myxomas, fibromas, and **psammomas,** occur, but these have been sufficiently described under **Tumours** (*see* pp. 288 and 339).

A neoplastic formation due to a developmental intermingling of nerve-cells " dislocated " from their proper environment, with consequent over-growth of neuroglia in the affected areas, has been described under the term **tuberose sclerosis.** The growths are multiple and found specially in the cortex. They are associated with congenital tumours in the brain, heart, kidneys, skin, and, less commonly, in other organs. An interesting report of a case is given by Fowler and Carnegie Dickson.[1]

Cancers.—Primary Cancer is rare, but may occur in connection with the ependymal lining of the ventricles or of the pineal body (*see* p. 861). **Secondary cancer** is also rare. **Endo-** or **Meso-theliomas,** secondary to tumours of the lung, as well as hypernephromata and chorion-epithelioma, have been described.

Cholesteatoma or " **Pearl-Tumour,**" which occurs occasionally in the membranes, is excessively rare in the substance of the brain. It is composed mainly of laminated layers of squamous epithelial cells, and contains usually a central mass of cholesterol-crystals. It is supposed to originate from the ependyma of the ventricles. Ziegler mentions the presence of small hairs in these tumours, and regards them as **dermoids.**

PARASITES :—

Echinococcus-cysts are not infrequent, especially in Australia; and *Cysticercus cellulosæ,* the immature or bladder-worm stage of *Tænia solium,* has also been found in the brain. In cases of **malignant malaria** the parasites, and considerable accumulations of pigment, may be found in the capillaries.

Secondary **Entamœbic abscesses,** as a complication of tropical dysentery, have been described, and, in these, the *Entamœba histolytica* has been found.

DISEASES OF THE CRANIAL NERVES :—

The cranial nerves are pressed upon and infiltrated by tumour-growth, by tuberculous meningitis or by syphilitic meningitis or gummata; and inflammatory or degenerative changes may result. The nature of these changes will be described later under **Peripheral Nerves,** p. 1013.

Optic Neuritis.—Inflammation in the optic nerve may occur at any part of its course, and may affect the connective tissue between the nerve-bundles (**interstitial neuritis**) or the nerve-sheath (**perineuritis**).

In **interstitial neuritis,** the cellular exudate presses upon the nerve-fibres, and, as the inflammatory exudate occurs most commonly in irregular areas (islets), special bundles of nerve-fibres—*e. g.* the macular

[1] " Tuberous (Tuberose) Sclerosis," Fowler and Carnegie Dickson, *Quart. Jour. Med.,* vol. iv., 1910, p. 43.
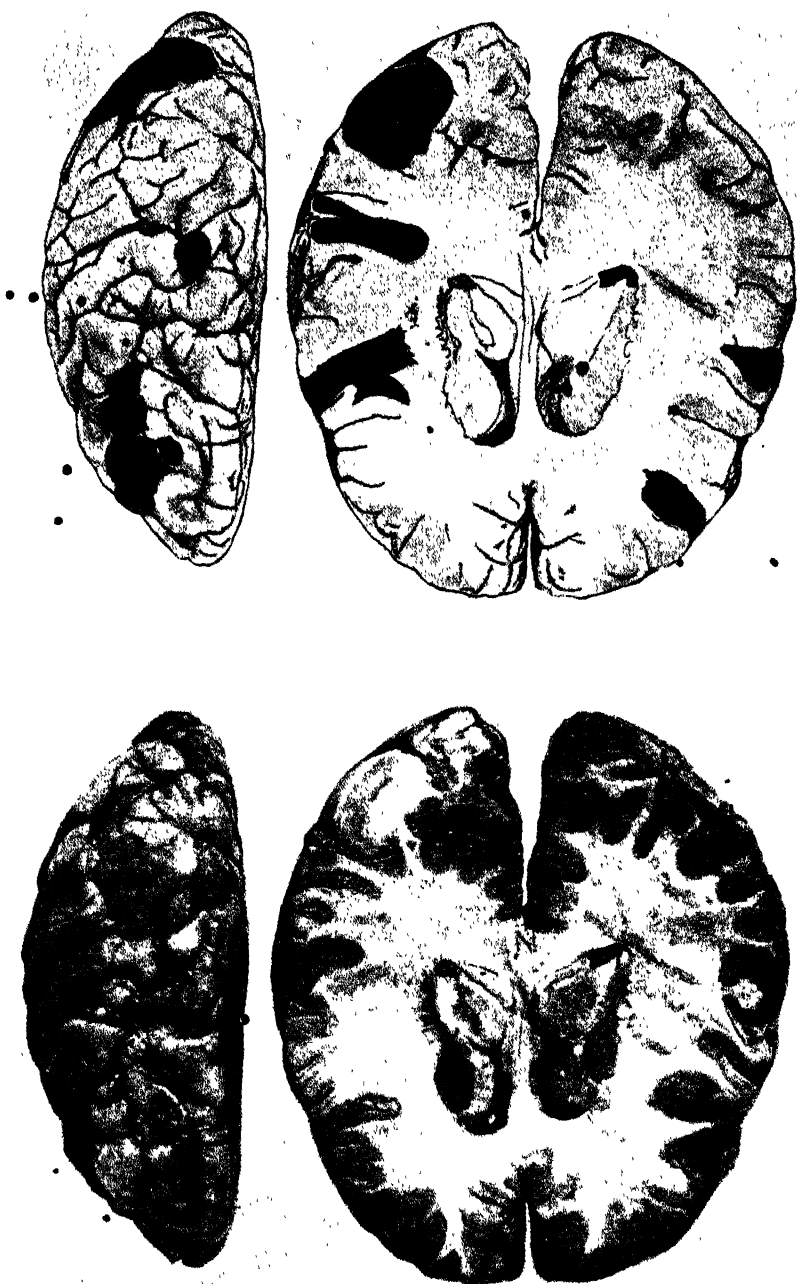
Fig. 452.—*Tuberose Sclerosis.* Shewing the nodules of tumour in the brain. In order to indicate these more clearly, their position is shewn in black in the outline sketch above. Note the small nodules in the walls of the lateral ventricles, as well as the larger masses in the grey and white matter towards the surface of the hemispheres. (Fowler and Carnegie Dickson's case.)

bundle—are not infrequently implicated. The nerve-fibres undergo degeneration—the medullary sheaths become broken up into fatty globules, and the axis-cylinders become varicose and, finally, disintegrate.

In **perineuritis,** the exudation takes place into the nerve-sheath, and is usually the sequel of an inflammation spreading from the meninges.

In both forms, cicatricial contraction may follow, and secondary degenerative changes in the whole nerve, leading to **optic atrophy,** may ensue.

Inflammation of the nerve below the entrance of the retinal vessels causes pressure on the retinal vein, and is followed by **œdema** of the nerve-head and surrounding retina. This condition- **papillitis**—is frequently accompanied by hæmorrhages into the retina. The fluid exudate collects between the nerve-fibres, and, as the disease progresses, the axis-cylinders in the neighbourhood of the papilla become broken up. The exudate may spread over the surrounding retina. Secondary sclerosis in the retinal vessels, with retinal degeneration, may occur.

Pressure upon the nerve at its entrance into the globe, by fluid collecting in the nerve-sheath, may cause obstruction to the venous return, and thus produce an intense **œdema** of the papilla—a condition known as **choked disc.**

DISEASES OF THE SPINAL CORD AND ITS MEMBRANES

Normally, the sub-arachnoid space, the ventricles of the brain, ànd the central canal of the spinal cord, form a continuous lymph-space. The central canal of the cord presents considerable variations. Typically, it is a narrow slit lined with cylindrical ependymal epithelium, outside which is a cellular layer of neuroglia.

Under pathological conditions, the canal may be widened or obliterated. As in the brain, dropsy of the cord may occur—the accumulation of fluid being either in the meninges or in the central canal. The latter form is called **Hydromyelia.** Cavities are sometimes found in the cord, which do not communicate with the central canal, but which have a similar structure. These probably arise from the original canal in the process of its development.

CONGENITAL ABNORMALITIES :—

(*a*) **SYRINGOMYELIA** is essentially the presence, in the spinal cord, of a cavity or cavities not completely lined with cylindrical epithelium. Various hypotheses have been propounded to explain the conditions which are found, but we do not propose to deal with these, as we regard the disease as a congenital defect in the development of the spinal cord. The cord is often very irregular in shape; the cervical region, especially, may be enlarged and flattened, though the upper dorsal region also may shew similar changes. The abnormality sometimes extends upwards to the medulla and, rarely, to the pons. The cavity in the cord may be single, or two cavities may be present side by side. In some cases, the diameter of the cavity is very small, while in others, the cavity is not apparent. On section, a mass of gelatinous material, pale or translucent, is seen surrounding the cavity. On **microscopical examination,** this gelatinous area is found to be composed of proliferated neuroglial tissue, varying considerably in amount in different cases, and at different levels in the same case. It forms a thin layer lining a large cavity, or a thick layer with a very small slit-like cavity in the centre, or a dense layer without any evidence of cavitation. This gliomatous tissue—is composed of varying proportions of neuroglial cells and fibres. Areas of degeneration are sometimes present, and, in these areas, both nerve-cells and nerve-fibres may be extensively degenerated. The nerve-roots, especially the anterior spinal-roots of the cervical enlargement, are also usually involved; and secondary degeneration of the nerve-tracts—sclerosis of the pyramidal tracts, posterior columns and ascending antero-lateral tracts—is a frequent

occurrence. **A typical** case may shew either the cavity-formation slight in degree, and the overgrowth of neuroglia very considerable: or the cavity-formation extensive, and the overgrowth of neuroglia very slight. Occasionally, the cavity communicates with the central canal.

(b) **SPINA BIFIDA.**—In this form of congenital malformation, the arches of certain of the vertebræ, with the ligaments, etc., are more cr less incomplete, and, through them, the spinal cord may present itself in one of two ways :—

1. **Closed Spina Bifida.**—There may be, projecting from the back, a rounded swelling, situated most frequently in the lumbo-sacral region
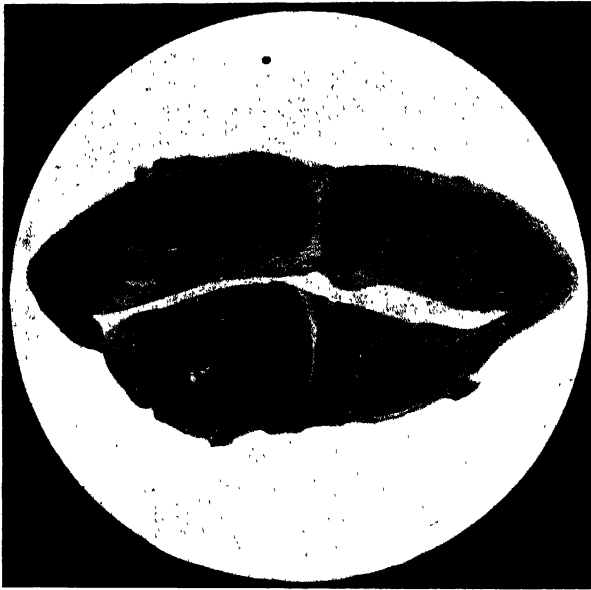

FIG. 453.—*Syringomyelia or Gliosis of Cervical Region.* Shewing the irregular cavity, with its neuroglial boundary-layer. (Pal-Weigert Method.) × 6.

of the spine. This mass is covered with skin over the greater part of its posterior surface, but usually, in the centre, the covering is completed by a membrane from which the skin-elements are absent. Beneath the skin are the membranes of the cord, or, generally, the pia-arachnoid alone—the dura being often absent. At the centre of the covering, in some forms of the malformation (**meningomyelocele**), a dimple is sometimes seen, which corresponds with the adhesion of the spinal cord or cauda equina to the inner surface of the sac. The centre of the dimple may contain an opening which communicates directly with the central canal of the cord. This form of spina bifida is really a dropsy of the cord. If the accumulation of fluid is between the membranes and the cord, the former alone are protruded (**meningocele**) and

the sac is lined by arachnoid and covered outside by skin. In **meningo-myelocele,** which is said to be the most frequent form of the abnormality, the cord and nerve-roots are pushed backwards, and a swelling is formed by an accumulation of fluid in front of the cord in the arachnoid sac. The cord itself and its nerve-roots are protruded and form the posterior wall of the sac. The sac is thus lined anteriorly and laterally by arachnoid and posteriorly by pia. In some cases, the protrusion consists of the dilated and closed central canal **(syringomyelocele)**—the sac, in this form, being lined by a thin layer of nervous tissue.

2. **Open Spina Bifida.**—In this condition, neither the development of the integument nor that of the medullary canal has been completed in the middle line, and the spina bifida is shewn by a groove, at the bottom of which is a membrane representing the open central canal of the cord. The tissue of the cord itself, throughout the open part of the spinal canal, is either absent, or present in very small amount. This condition may be accompanied by anencephaly, the fœtus being then non-viable.

CALCAREOUS DEGENERATION sometimes occurs, appearing in the form of thin pearly-white plates, often shewing concentric lamination, and possessing sinuous or very irregular edges, which are continuous with the membrane in which they occur. They are found, as a rule, in the pia-arachnoid of the cord or nerve-roots, and generally give rise to no symptoms during life.

INFLAMMATION :—

(a) **Of the Dura-Mater.**— Inflammation of the external surface of the dura may be the result of the direct extension of the inflammatory process from neighbouring structures, for example, an abscess in bone, or a septic focus such as a bed-sore. The condition may be suppurative, and the spinal canal become filled with semi-purulent fluid, which is commonly mixed with blood. The dura-mater is swollen, and dark-greenish or livid in colour. The pia and the arachnoid generally become secondarily infected.

Inflammatory changes confined to the inner surface of the dura are not common.

Pachymeningitis hæmorrhagica interna may occur in cases of insanity, but, in the spinal canal, is much rarer than the corresponding condition in the cranium (see p. 951).

Pachymeningitis hypertrophica is a rare condition which is seen in the cervical region of the cord. The inner surface of the dura becomes gradually thickened by the formation of concentric layers of fibrous tissue. Adhesion to the pia-mater, which also is thickened, is common. The condition causes pressure-atrophy of the nerve-roots from narrowing of the spinal foramina, together with secondary changes both in the cord and in the peripheral nerves. In some cases, the condition is syphilitic in origin.

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(b) **Of the Pia-Mater.**—We include with the pia-mater the arachnoid, which, though not in such intimate association with it in the cord as in the brain, yet, generally, is associated with it and exhibits similar changes in disease. Spinal **Leptomeningitis** is frequently secondary to cerebral meningitis. Sometimes, however, it may arise independently, as a result of local inflammatory processes, which, by their extension upwards, lead to a secondary involvement of the cerebral meninges. The pia is swollen and injected, and numerous small hæmorrhages are seen in it. The arachnoid is congested, and there is excess of fluid—at first clear, but later semi-purulent—in the sub-arachnoid space. The exudate, if purulent, is usually most abundant on the posterior surface of the cord. The change may spread to the dura, or, more commonly, to the spinal cord itself, giving rise to myelitis. Spinal leptomeningitis may be due to the organisms which have already been enumerated as causing cerebral meningitis—*Streptococci, Pneumoccci, Meningococci,* and *B. tuberculosis,* being among the more important of these.

Localised collections of fluid in the meninges, simulating cysts (**meningeal cysts, meningitis serosa**), are comparatively rare and are due to focal meningitis.

TUBERCULOSIS.—For descriptive purposes, tuberculosis of the spinal cord and of its membranes cannot be separated from one another. Several varieties of the condition occur.

1. **Tuberculous meningitis associated with caries of the vertebræ.** Tuberculous caries may be limited to one vertebral body, or it may affect several. Occasionally, it commences in the transverse process and secondarily affects the vertebral body. It is found at any part of the spinal column, but is of most frequent occurrence in the lower dorsal and upper lumbar regions. The tuberculous infection, after destroying the anterior common ligament, reaches the dura, the outer surface of which becomes greatly thickened and infiltrated. The tubercle-granulations extend into the substance of the dura, and, at a later period, give rise to extensive tuberculous infiltration of its inner surface. Further extension takes place, and the pia-arachnoid and the various nerve-roots become involved. On account of the accumulation of tuberculous material in the canal, compression of the spinal cord (*see* fig. 463), with consequent ascending and descending degenerations, may follow. By reason of the destruction of the vertebral bodies, curvature of the spine with displacement of, and pressure on, the spinal cord, takes place, and myelitis is produced. Death supervenes, in some cases, from sudden dislocation of the diseased vertebræ. This is especially the case where the odontoid process, or the transverse ligament which holds it in position, becomes eroded by the disease. In cases of tuberculous caries (Pott's disease), localised patches of myelitis or myelitic degeneration may occur even apart from pressure. These are due probably to interference with the blood-supply (ischæmia) or to the action of the toxins.

2. **Tuberculous pachymeningitis,** unassociated with disease of the bone, sometimes occurs, especially in the cervical region of the cord. The dura-mater and the surrounding structures become greatly swollen and infiltrated with tubercle-granulations.

3. **Tuberculous leptomeningitis.**—This is, as has been stated, generally associated with tuberculous cerebral meningitis, and is very frequently the starting-point of that condition—the infection having reached the spinal membranes, from the abdomen or thorax, by way of the lymphatics. Minute, grey tubercle-granulations are seen on the surface of the pia-mater, at first especially in the cervical or the lumbar region, but, later, throughout the whole length of the cord, among the nerve-roots of the cauda equina, and also on the inner surface of the dura. The subarachnoid space may be distended with fluid which is usually rich in lymphocytes. *B. tuberculosis* is often only with difficulty demonstrated in the fluid; but is found, sometimes in enormous numbers, in the granulations in the meninges.

4. **Tuberculous granulations** are very rarely found in the **substance of the cord** itself without primary affection of the meninges. When present, they are usually in the form of large, solitary, conglomerate tubercles, which give rise to areas of softening and myelitis (myelomalacia).

SYPHILIS.—The conditions in the cord produced by syphilis are analogous to those seen in the brain. There may be marked **thickening of all the membranes,** with involvement of the nerve-roots, and, usually, associated myelitis (meningo-myelitis). **Syphilitic endarteritis** and **peri-arteritis** are always well marked. **Gummata** develop from the inner surface of the dura, or from the pia-arachnoid, and cause pressure upon, and softening of, the cord. Sometimes, but much more rarely, the gummata are found in the substance of the cord. Degenerations caused by syphilis in the conducting tracts will be dealt with later.

INJURIES OF THE CORD are rare, except in cases of fracture or dislocation of the spine, and in gunshot and other wounds, in which lesions the tissue may be lacerated, crushed, or even torn across.

CONCUSSION OF THE CORD, if severe, may give rise to a condition of degeneration, with paralysis of limbs, etc.

HÆMORRHAGE into the cord is rare, except in cases of direct injury.

Petechial hæmorrhages may occur as a result of severe concussion, and are frequently found around an area of acute softening—and these or larger hæmorrhages have been described in **shell-shock,** in **scurvy,** in **cerebro-spinal meningitis,** etc. Hæmorrhage into or on the meninges is found as a direct spread from hæmorrhage into the brain.

INFLAMMATION (MYELITIS) :—

The terms **myelitis** and **myelomalacia** are commonly applied, more or less promiscuously, to any **softening** of the spinal cord. The former term is often inaccurately used in this connection, as, in many cases, the

condition is not a true inflammation, and is due to pressure, or to mechanical interference with the blood- and lymph-supply.

Causation :—

1. **Such primary softening of the cord** results from the action of bacterial toxins or other poisons. It either occurs in irregular patches, or in the lines of definite nerve-tracts. This condition sometimes follows such acute infective diseases as typhoid fever, influenza, pneumonia, dysentery, etc. It is said to occur as the result of cold and chill, but these are to be regarded as only predisposing causes. Alcoholic subjects are said to be specially liable to myelitis; and syphilis, quite apart from the formation of gummata, is regarded by some authors as causal.

2. A similar condition may follow **injuries** to the cord : **pressure** upon it by tumours, tuberculous masses or abscesses, syphilitic gummata or meningitis : and **infiltration** of its substance by tuberculous masses, syphilitic gummata, tumours, inflammatory exudates, etc.

3. It may result from vascular obstruction, whether produced by pressure on the vessels from outside, or by embolism, or by thrombosis in degenerated, often syphilitic, vessels.

The condition may be **disseminated,** appearing in scattered areas, or extending throughout considerable portions of the cord without involving its whole diameter : or **transverse,** affecting a limited length of the cord, but involving its whole thickness. The transverse form may be the result of direct injury in fractures or dislocations, or of pressure on the cord, though in some cases its cause is obscure. The diffuse or disseminated variety is the usual form seen in acute infectious diseases.

Characters of the Lesion.—There is usually a varying of **engorgement of the vessels of the pia,** especially over the affected area which is itself intensely **congested** and extremely **soft**—sometimes **diffluent** or semidiffluent. Numerous minute **hæmorrhages** may be present, and in some cases there is a moderate degree of **meningitis.** The normal markings, and the differentiation of the component parts of the cord, cannot be made out. In the later stages of the forms due to pressure, the congestion subsides, and the softening, becoming more marked, spreads both up and down the cord.

On microscopical examination, the blood-vessels are seen to be distended, and round them, in the perivascular spaces, are accumulations of leucocytes, mainly of the lymphocyte-type; but polymorphonuclear leucocytes, plasma-, and mast-cells may be present. Masses of pigment are sometimes found in the neighbourhood of the vessels. The neuroglia-cells are swollen, vacuolated and multinuclear, and, if the process is slowly developed, the neuroglia itself is increased and the nerve-tissue relatively diminished. On transverse section, the nerve-fibres are seen to present great variations in their diameter, some being considerably swollen; whilst others are atrophied and somewhat granular in appearance. The axis-cylinder may be enlarged, broken up into granular masses, or even absorbed; the myelin-sheath distended and narrow, or broken up

Fig. 454.—*Normal Nerve-cells.* Showing the central position of nucleus, the Nissl-granules, and the protoplasmic processes. (Nissl's Method.) × 300.

Fig. 455.—*Degenerated Nerve-cells.* Shewing eccentric position of the nucleus, and disappearance of the Nissl-granules and of the protoplasmic processes. (Nissl's Method.) × 300.

and granular. The cells in the grey matter shew degenerative changes, are swollen, and rounded in outline, the nucleus becomes eccentric and stains less intensely, and there is perinuclear, or perhaps complete, disappearance of the Nissl-granules. The protoplasmic processes may shew various stages of degeneration, from slight alterations in structure up to complete disappearance. Areas of secondary degeneration are seen extending for a variable distance both above and below the affected area. The whole diseased area often becomes infiltrated with leucocytes and degenerated neuroglial cells—the so-called compound granular corpuscles.

In extreme cases, film-preparations shew fat-droplets, compound granular cells—probably neuroglia-cells which have ingested disintegrated myelin and fragments of axis-cylinders—leucocytes, degenerated and vacuolated nerve-cells, granular detritus, and, sometimes, bacteria.

In cases in which the lesion is brought about by gradually increasing pressure, the changes are less acute than those described, and the grey matter suffers to a less degree than the white.

•Ascending and descending degenerations in the implicated spinal nerve-tracts, paralysis and wasting of muscles, bed-sores, and cystitis and pyelitis from paralysis and infection of the bladder, are usual accompaniments of acute myelitis.

The condition frequently becomes chronic; the fat, the granular cells, etc., are absorbed; and a so-called **grey softening** results. In this stage, there is proliferation of the neuroglial tissue—sclerosis—and the nerve-fibres and the nerve-cells to a large extent disappear. The neuroglial tissue appears looser and more open. Retraction takes place, and, eventually, the softened area is replaced by a cicatrix or pseudocyst, and the motor and sensory conduction in the cord is interrupted.

ACUTE ANTERIOR POLIOMYELITIS (INFANTILE PARALYSIS).

This is a specific infective and contagious disease, attacking especially infants and young children, and is due to an ultra-microscopic organism which can be obtained from the spinal cord of persons who have died from the disease and from the cord of monkeys which have been experimentally infected with the virus, and which have developed the disease. The organism has been grown on artificial media by Noguchi. Epidemics have been observed in many countries; and carriers, in whom the causal organism is lodged in the naso-pharynx, are definitely recognised as agents in the transmission of the disease. In the **earlier, acute stage,** the pia-mater is actively congested, and the sub-pial fluid considerably increased in amount. There is, frequently, definite meningitis. Both the grey and the white matter are acutely congested—the grey usually more than the white—and areas of softening may be detected. There is marked cellular infiltration with polymorphonuclear and other cells, in, and around, the walls of the blood-vessels, and

areas of hæmorrhage are not infrequently seen. The motor cells, in the affected areas in the anterior horns of the cord, undergo degenerative changes. The cells have a cloudy appearance and are slightly swollen, and the chromophil granules appear to be larger than in the normal cells. The nucleus may shew chromatolysis, the chromatin eventually disappearing, and the cytoplasm becoming granular and vacuolated. **At a later stage,** the affected cells become completely disintegrated. The non-medullated nerve-fibres are swollen, the neuroglia is increased, and there may be considerable infiltration with lymphocyte-like cells—these often collecting especially round the disintegrated motor-cells. The lesion is usually confined to one side, but is occasionally bilateral. The changes are
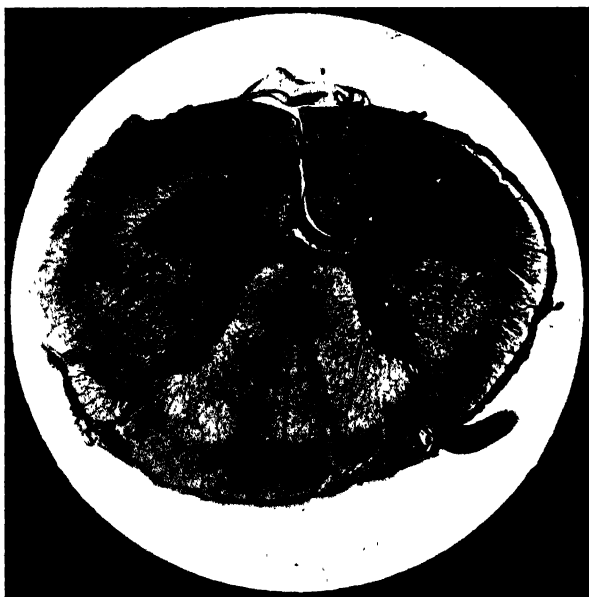

Fig. 456.—*Section of Cord in the Cervical Region.* From a case of Infantile Paralysis, shewing the atrophy of one anterior horn and changes in the white matter in the neighbourhood. (Stained with carmine.)   × 5.

found in the lumbar region when the paralysis affects the leg, and in the cervical region when the arm is involved. Part, or the whole, of the anterior horn may shew degenerative changes; in the anterior commissure, partial destruction of fibres is sometimes found; and the anterior nerve-roots and the muscular branches of the peripheral nerves are atrophied.

In **old-standing cases,** the affected anterior horn, or part of it, is much smaller than that of the opposite side. Motor-cells—usually in diminished numbers—may still be present, some of them shewing a peculiar colloid character, due to imbibition of fluid: others shrunken and degenerated: and others, again, apparently normal. The localisation of motor functions to the various groups of nerve-cells in the anterior

Fig. 457.—*Healthy Betz-cells.* Shewing nucleus and nucleolus (one cell), cell-processes and Nissl-bodies. (From specimen lent by Drs. Watson and Bigland, Liverpool.) × 300.
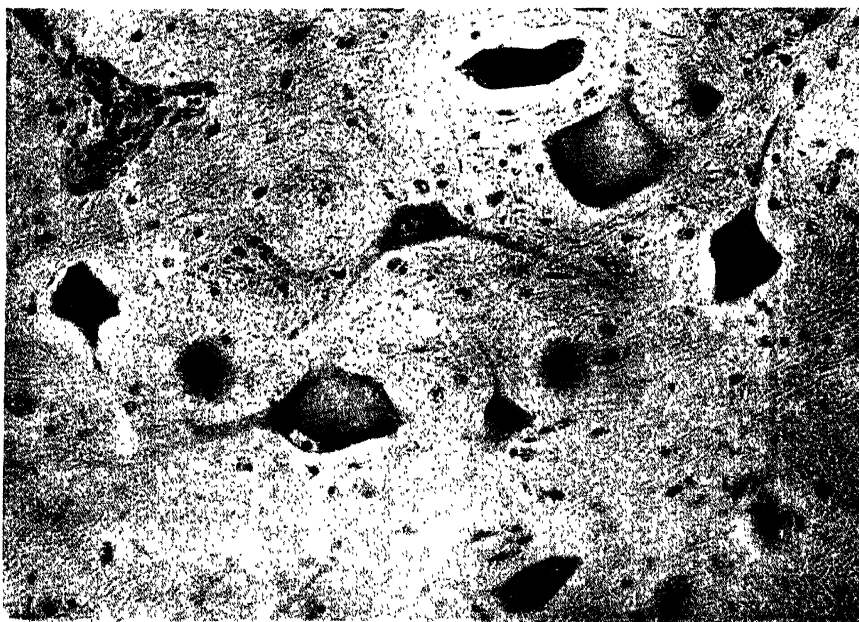

Fig. 458.—*Degenerated Nerve-cells.* From the anterior horn of the spinal cord in a case of Pellagra, shewing eccentric position of nucleus, disappearance of Nissl-bodies, loss of processes, etc. (Lent by Drs. Watson and Bigland, Liverpool.) × 300.

horn furnishes the explanation of the limitation of the paralysis to certain combinations of muscles—for a study of a series of cases proves that certain groups of cells, as we have stated, are shrunken and degenerated, whereas others are apparently uninjured. There is, usually, a great increase of neuroglia, the delicate fibrils of which form a loose reticulum. The nerve-fibres are almost completely absent. In some cases, the only change is in the motor-cells and the delicate nerve-fibres—the neuroglia showing no variation from normal. The blood-vessels are sometimes thickened, and the perivascular spaces dilated. In all cases, there is descending degeneration of the motor-fibres associated with the

Fig. 459.—*Section of the Cord in the Lumbar Region.* From a case of Poliomyelitis. (Pal-Weigert Method.) × 8.

affected cells; and the muscles with the function of which interference has occurred, also undergo degeneration—the muscle-fibres becoming atrophied and occasionally replaced by fat. The other tissues—bones, blood-vessels, etc.—share, to a greater or less degree, in this atrophy, or—more accurately—in this atrophy combined with impaired growth and development.

POLIO-ENCEPHALO-MYELITIS.—This name is given to cases of anterior poliomyelitis complicated by lesions in the cerebrum, such, for example, as hæmorrhages below the level of the corpora quadrigemina (Wernicke's disease), or acute bulbar myelitis with lesions extending above the bulb. In such cases, the nerve-tracts in the cerebral white matter are involved. Batten considers many of these cases to be due to thrombosis of the small terminal vessels, and that this thrombosis, which may occur both in the brain and in the cord, is bacterial or toxic in origin.

ACUTE ASCENDING PARALYSIS (LANDRY).—This disease is characterised clinically by the occurrence of rapidly developing paralysis, extending from below upwards, and without sensory disturbances, death supervening, as a rule, from involvement of the bulbar nuclei. Our knowledge of its **morbid anatomy** is still very indefinite, and the lesions found seem to vary in different cases. There may be no obvious naked-eye changes in the brain or spinal cord beyond a few capillary hæmorrhages. Buzzard states that, on careful examination, especially in rapidly fatal cases, a varying number of the **motor cells** of the anterior horns and of Clarke's column shew chromatolysis, or more or less complete loss of chromatin, and excentration of nuclei; whilst the **myelin-sheaths** of the spinal nerve-tracts and of the peripheral nerves present a diffuse fatty change. The **vessels** are engorged, but there are no special peri-vascular changes, and the **neuroglia** shews no evidence of proliferation. The similarity of the symptoms to those of acute anterior poliomyelitis, and the character of the changes found in the nerve-cells of the anterior horn of the cord, suggest that the disease is really a very acute form of anterior poliomyelitis produced by some powerful bacterial or chemical toxin, and that death occurs before marked cell-degenerations and cell-infiltrations become manifest.

DEGENERATIVE CONDITIONS OF THE CORD :--

In this group, we include a series of diseases which are characterised by a more or less complete destruction of certain conducting **tracts** and **groups of nerve-cells in the spinal cord,** and in which the processes which bring about the pathological changes appear to be degenerative rather than inflammatory, though, in some of them, there has been described the occurrence of a preliminary, or, perhaps, antecedent, acute disease. The causes of many of these changes are still unknown, though some of them are undoubtedly syphilitic. The degeneration may be limited to one tract, or to one group of nerve-cells; but, very commonly, combinations take place, two or more tracts possessing different functions, or certain conducting tracts and certain groups of nerve-cells, being involved. The degeneration may be ascending or descending, according as sensory, motor, or communicating tracts are affected. To understand the changes thoroughly, an accurate knowledge of the anatomy and physiology of the spinal cord must first be obtained, but for this we refer our readers to textbooks of Anatomy and Physiology or Neurology.

A.—PROGRESSIVE MUSCULAR ATROPHY or POLIOMYELITIS ANTERIOR CHRONICA (ARAN-DUCHENNE).—This disease, especially occurring in adults, commences in the anterior horns of the grey matter of the spinal cord, usually in the cervical region. Beginning in one horn, the condition tends to spread to that of the opposite side.

The nerve-cells become shrivelled and lose their processes, whilst the nuclei lose their affinity for basic stains. This degeneration and eventual disappearance of the motor cells of the anterior horn, which itself may remain unaltered in outline, are associated with a disappearance of the fine nerve-fibres, and a moderate degree of overgrowth of the neuroglia, seen in the form of a meshwork of fibrils, among which are numbers of spider-cells. There is marked degeneration of the anterior nerve-roots and, to a less extent, of the peripheral motor-nerves, the nerve-fibres connected with the degenerated nerve-cells being specially picked out by the change. In some advanced cases, the nerve-fibres in the anterior nerve-roots may have almost completely disappeared, and been replaced by connective tissue.

The atrophy may commence in the lower group of cells in the lumbo-sacral region, and then spread to all the groups in the lumbar enlargement; it, in some cases, extends upwards from the lumbo-sacral region until all the motor-cells in the cord are affected; or it may, at first, be limited to certain groups of cells in the cervical region—especially those parts which govern the muscles of the hand—but, in these cases, it soon spreads to all the cells in the cervical enlargement. In this latter group of cells, in which the atrophy is the commonest, the muscles first affected are usually those of the thenar and hypothenar eminences, the interossei, and then the muscles about the shoulder; but, in some cases, the condition spreads gradually and progressively to the other muscles of the limbs and trunk. The muscles undergo atrophy, and sometimes fatty changes— scattered individual fibres, or groups of fibres, being picked out in accordance with the distribution of the ·degenerative changes in the corresponding motor nerve-cells. The sarcolemma-cells undergo proliferation, and connective tissue is formed to replace the atrophied muscular tissue. In other cases, **microscopical examination** shews a simple atrophy of the fibres, without special deviation from their normal structure. The muscular changes become more advanced as the degenerative processes in the cord and in the motor nerves progressively spread.

PERONEAL TYPE OF MUSCULAR ATROPHY.--This chronic form of muscular atrophy is often hereditary—several members of a family may suffer from it, and the disease may be traced through several generations. By many, the condition is regarded as a chronic multiple neuritis : by others, as a spinal disease due to an ascending degeneration of the peripheral motor-nerves, degeneration of spinal ganglia and atrophy and loss of the nerve-cells in the anterior horn of the spinal cord, the anterior and posterior nerve-roots, the fibres in the posterior columns and even the motor-cells in the anterior cornua. Sclerosis has been found in the posterior columns, particularly in the postero-external. The intramuscular fibres, especially of the peripheral motor-nerves shew marked degeneration, and, at a late period, the sensory nerves are also affected.

Pseudo-hypertrophic Muscular Paralysis is a disease which, in some respects, resembles progressive muscular atrophy; but, as no definite lesion has been detected in the spinal cord, it is now generally held that it is a primary affection of muscle. The disease appears to be hereditary, and attacks especially male children. There is atrophy of the muscular substance, with a new formation of connective and adipose tissue between the fibres. The new formation may be so great that the bulk of the atrophied muscle is increased —hence the term "pseudo-hypertrophic" applied to the condition. In the later stages, no trace of muscle-fibres may be detected in the affected area. The muscle-fibres, when still present, may retain their transverse striation. In some cases, the muscle-fibres shew proliferation of the nuclei, vacuolation, splitting, and, often, a hyaline appearance. The lower limbs, especially the muscles of the calf, are generally the first to be involved, the condition spreading more widely later. (*See* pp. 1059–60.)

B.—AMYOTROPHIC LATERAL SCLEROSIS.—In this disease, there is a degeneration of the pyramidal tracts, of the nerve-cells of the anterior horns of the spinal cord, of the anterior roots, of the peripheral nerves,

Fig. 460.—Very extensive Sclerosis of the Spinal Cord (the pale part is the sclerosed portion.) (Pal-Weigert Method.) × 6.

and of the muscles. The degeneration does not usually extend above the pons, but cases have been described in which the changes reach the cerebral peduncle, the internal capsule and even the motor-cortex. Not uncommonly, there is also degeneration in the antero-lateral columns —between the anterior horns and the surface of the cord; and, in some cases, there is also evidence of degeneration in the posterior columns —especially the postero-median column of Goll. Degeneration of the middle third of the corpus callosum has been described. The cord may be diminished in size, especially in the cervical region. The dura shews no obvious pathological change, the substance of the cord itself is very firm in consistence, the hypoglossal and glosso-pharyngeal nerves and the anterior

spinal nerve-roots are thin and atrophied, and the pyramidal tracts are of a greyish colour. The condition is sometimes confined to the cervical region, but frequently the lumbar region is affected, and occasionally the entire cord. In the majority, at any rate of advanced cases, there is degeneration, with atrophy, of the giant-cells of Betz in the precentral gyrus, these cells being the **neuron-bodies** of the cortico-spinal elements of the motor-system. According to Starr, this degeneration of the cortico-spinal elements begins in the ends of the axons in the spinal cord, and advances upwards until the whole neuron becomes atrophied. The atrophied nervous elements are replaced by neuroglial tissue.

On microscopical examination, varying degrees of advanced sclerosis are seen in the affected areas. The contour of the horn is usually maintained, but the cells in it are scanty and shrunken, the nuclei absent or

Fig. 461.— An irregular area (pale) of Sclerosis in the Spinal Cord.
(Pal-Weigert Method.)   × 6.

displaced, the protoplasmic processes thin, short, or entirely absent, and the chromophilic elements (Nissl-granules) either entirely destroyed or remain merely perinuclear in distribution. The changes in the medulla are often marked, and the cells of the hypoglossal nuclei may shew degenerative changes. Other nerve-nuclei (trigeminal, facial, glosso-pharyngeal, etc.) may share in the changes. The neuroglia is but slightly increased. The peripheral nerves, and the muscles supplied by them, shew a varying degree of atrophy, according to the extent of the lesion in the cord.

C.—**DISSEMINATED or INSULAR SCLEROSIS.**—In this condition, the cord is usually not altered in size, though it may be somewhat shrunken

and firmer in consistence at the level of the degenerated areas. The pia-mater may be adherent to the cord. **On section,** there are greyish patches, somewhat gelatinous in appearance and with rounded or angular outlines, scattered irregularly throughout the cord, and commonly associated with similar changes in the brain. **On microscopical examination,** numerous leucocytes and proliferated cells are found in the peri-vascular spaces. The walls of the vessels, especially of the arterioles, may become thickened, and, in them, the newly-formed fibrous tissue may present a homogeneous appearance, sometimes described erroneously as " hyaline " degeneration. The neuroglia is usually greatly increased in amount, glial fibres and the glial cells forming a dense network, and there may be some increase of connective tissue especially round the vessels. The medullary fibres are, at first, swollen—the myelin-sheath being fragmented and the neurilemma-nuclei shewing considerable swelling. Later, the myelin breaks down and is absorbed, and the sheath blends with the surrounding tissue. The axis-cylinder is, at first, irregularly swollen, and has a beaded appearance. Eventually, it becomes broken across and is absorbed. Usually, however, some axis-cylinders persist. This form of **sclerosis** does not tend to spread, but may, in virtue of its position and the destruction of the axis-cylinders, interfere with the conducting tracts of the cord, and give rise to secondary degeneration in these tracts. The sclerosis affects both the grey and the white matter of the cord.

D.—**SUBACUTE COMBINED SCLEROSIS.**—This condition has been described as occurring in association with severe anæmia, especially in pernicious cases. Sclerosis may be evident in the posterior columns, and sometimes in the region of the crossed pyramidal tracts. The changes are observed especially in the mid-dorsal region of the cord. There is degeneration of the myelin-sheath and disappearance of the axis-cylinder. The area becomes invaded with compound granular corpuscles and, later, there is an overgrowth of fibrous tissue.

E.—**PRIMARY LATERAL SCLEROSIS (SPASTIC PARAPLEGIA),** which is extremely rare, consists in complete degeneration of the crossed pyramidal tracts on each side. The degeneration begins in the external portion of the lower part of the crossed pyramidal columns, and, gradually, the axons atrophy from below upwards and disappear; and are replaced by a secondary hyperplasia (sclerosis) of the neuroglia.

The change may spread throughout the whole cord, or be limited to a few segments, and extension to the anterior horns and the antero-lateral ascending and direct cerebellar tracts sometimes takes place.

Microscopical examination shews a **primary** sclerosis, with partial or complete disappearance of the nerve-fibres, an overgrowth of neuroglia, and, sometimes, a thickening of the walls of the blood-vessels.

F.—**LOCOMOTOR ATAXIA.**—By the majority of authors, this disease is regarded as of syphilitic origin. In many cases, however, it is difficult to trace a syphilitic infection. But the application of the Wassermann test to the cerebro-spinal fluid has shewn that a considerable proportion of cases give a positive reaction, though the reaction in the blood may be feeble or negative in an appreciable number of such cases. Various views are held as to its starting-point, some regarding it as a primary sclerosis of the posterior columns of the cord—Marie views it as a syphilitic lymphangitis of the posterior columns. Others hold that it is a primary degeneration of the sensory nerves, especially of their trophic nerve-cells in the ganglia on the posterior nerve-roots, and that the change in the cord is really an ascending degeneration. The neuron-bodies lying in the posterior spinal ganglia shew swelling, chromatolysis, vacuolisation, pigmentation and, sometimes, fatty degeneration, at any rate in advanced cases; and it has been shewn that the degeneration in the posterior columns affects chiefly the fibres (**exogenous fibres**) which enter them through the posterior roots. The association-fibres, which arise within the cord itself (**endogenous fibres**), from cells of the grey matter and connect the various segments with one another, are not affected in lesions of the posterior nerve-roots, and they always escape in locomotor ataxia. These facts strongly favour the view that locomotor ataxia is really a disease of the sensory neurons, producing degeneration of the exogenous fibres passing into the spinal cord from these neurons, and not a primary disease of the spinal cord itself.

In the cord, the changes are usually most marked in the posterior columns in the lumbar or dorso-lumbar region; but, in rare cases, the cervical region is affected. The spinal cord may be smaller in diameter than normal, the pia is occasionally thickened and adherent over small areas on the posterior surface; and the posterior nerve-roots may be diminished in size, the ganglia upon them shewing marked degenerative changes to be described presently. In other cases, the dura, pia, and posterior nerve-roots, may appear normal.

In the early cases, the changes are most marked in those parts of the external column which adjoin the posterior horns, and in the marginal zone (Lissauer). In relation to this distribution of changes, it should be noted that some of the fibres from the posterior nerve-roots enter at the apex of the posterior horn and turn upwards in the marginal zone (Lissauer) to enter the posterior grey matter at a higher level, whilst others turn downwards : further, that the fibres which degenerate earliest are the median fibres and their collaterals which are found mostly in the inner part of the postero-external column, and the fine fibres, referred to above, in the marginal zone (Lissauer). Again, the disease begins, in the majority of cases, in the neurons of the lumbar nerves, and, therefore, in the early stages of the disease the lumbar segments are principally affected; but, as the condition advances, a larger number of ganglia

are involved and a greater extent of tissue becomes degenerated in the posterior columns. At later stages, the posterior columns on each side may be affected to a varying degree in different parts of the cord. In the **cervical region,** the **whole posterior column** may be involved; or the degeneration may be confined to the **external part of the postero-internal column** *(Goll),* to the **postero-external column** *(Burdach),* and to the **marginal zone** (Lissauer). In the **dorsal region,** the changes are more marked in the **postero-internal column** (Goll); and, in the **lumbar region,** in the **postero-external column** (Burdach) and the **marginal zone** (Lissauer). The degeneration, when present in the **posterior nerve-roots,** may be traced to the **spinal ganglia**—the cells of which, as has already been
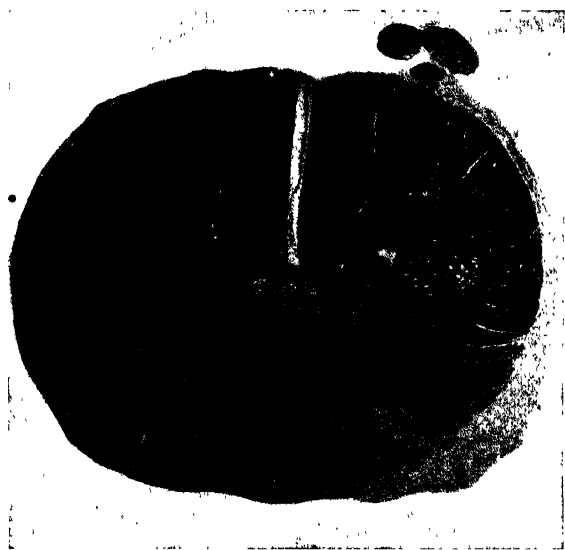
FIG. 462.—*Locomotor Ataxia.* Shewing the Sclerosis in the posterior columns. (Pal-Weigert Method.) × 6.

noted, may be shrunken, may stain very deeply, and shew excessive vacuolation, and a high degree of pigmentation. In advanced cases, there may be destruction of all the cells in the affected ganglia. The changes in the **peripheral,** the **cranial,** and the **sympathetic nerves,** are variable, but are all of a degenerative nature, the nerve-fibres being affected, and the connective tissue increased. It is the **sensory nerves** which are particularly implicated, more especially the fine filaments supplying the skin and joints. In the cord, the degenerative conditions, in rare cases, tend to spread transversely to the lateral columns but, frequently, there is some degeneration in the posterior horns of the cord, and, rarely, in the anterior horns.

, **Perforating ulcer of the foot,** enlargement of joints **(Charcot's Joint),** and other trophic disturbances, may be associated with the condition.

G.—HEREDITARY SPINAL ATAXIA (FRIEDREICH'S DISEASE).

This condition tends to occur in several members of the same family, beginning usually at an early age. The lesion is of a similar nature to that of locomotor ataxia, but, in addition, both the exogenous and the endogenous fibres are degenerated in the **crossed pyramidal tract,** and, generally, in the **direct cerebellar** and the **antero-lateral ascending tracts.**

Fig. 463.—Tuberculous (Pott's) Disease of bodies of Vertebræ, producing pressure on the Spinal Cord.

In the posterior columns, the **postero-internal tract** is affected throughout almost its entire length, and the **postero-external** to a much less extent. Almost the whole of the **crossed pyramidal tract** is degenerated. The cord is usually smaller than normal—this diminution in size being seen especially in the cervical region—and the pia is thickened. There is an increase of neuroglia, with atrophy of the nerve-fibres. The increase in connective tissue is comparatively insignificant. There is atrophy of the cells in both anterior and posterior horns; and the cells of Clarke's

column are notably degenerated. Atrophy of the posterior roots and of the peripheral nerves may occur, but is not constant. It is generally agreed that the disease is due to an arrest of development of various systems of fibres in the spinal cord.

H.—SECONDARY SCLEROSIS :—

Secondary degenerations in the cord may be the result of direct injuries to, or of lesions which press upon, the cord. Thus, fracture-dislocation of the vertebræ, tuberculous disease, tumour or aneurism, syphilitic gummata, or inflammatory exudates may, by pressure, or, in some cases,
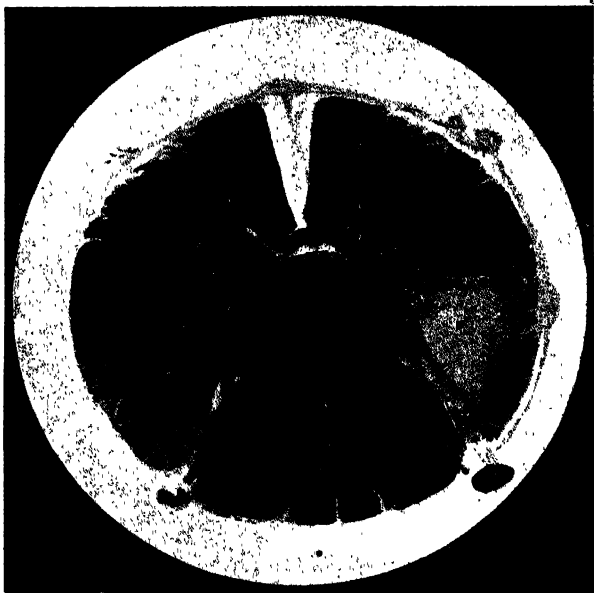
Fig. 464.—*Section of the Cord from a case of Hemiplegia.* Shewing secondary Sclerosis (pale area) in the crossed pyramidal tract. (Pal-Weigert Method.) ×6.

by direct invasion of the substance of the cord, be the cause of secondary degenerations. As a rule, however, the degenerations are due to interference with the descending tracts, or their centres in the brain, by hæmorrhage, softening, tumour-formation, etc. The main change is a destruction of the medullary sheaths. With the loss of the highly refractile substance of which these are composed, the nerve-fibres appear greyish in colour—grey degeneration. Microscopically, in the affected area, there is an increase in the neuroglia and a great reduction in the number of nerve-fibres. There may be, in addition, a new formation of connective tissue.

As a general rule, the degeneration follows the direction in which the nerve conducts, and, therefore, descending degeneration will be

found mainly in the direct and crossed pyramidal tracts; but, particularly after transverse lesions of the spinal cord, descending degeneration may also occur in other antero-lateral columns, *e. g.* the intermedio-lateral tract of Löwenthal, the sulco-marginal anterior descending tract of Löwenthal and Marie, in the descending comma-tract, and in other situations in the posterior columns; whilst **ascending degeneration** will occur in the posterior columns immediately above the lesion, if it is a transverse one in the cord; but, at a higher level, only the median columns (Goll) show degeneration.

Degenerative changes may be found also in the direct cerebellar tract, and the antero-lateral ascending tract, if the lesion is above the junction of the dorsal and lumbar regions. These degenerations may extend through varying lengths of the cord, depending upon the space which the various tracts occupy within it.

The commonest **descending degeneration** is that which occurs in the **pyramidal tracts** as a result of some lesion in the brain, affecting its motor nerve-cells, or the fibres as they pass downwards from these, *e. g.* a hæmorrhage into the internal capsule. The degeneration follows the fibres, and, therefore, will be seen in the following situations :—

1. On the same side as the cerebral lesion :
   (*a*) In the middle two-fifths of the crus.
   (*b*) In the pyramidal bundles between the superficial and deep transverse bundles in the pons.
   (*c*) In the anterior pyramid of the medulla.
   (*d*) In the direct pyramidal tract—the fibres affected in this situation being those which have not decussated at the point of observation, or which do not decussate.
2. On the side opposite to that of the cerebral lesion :
   (*a*) In the crossed pyramidal tract.
   (*b*) In the fibres of the direct pyramidal tract which have already decussated above the point of observation.

The **extent of the degeneration** becomes less as the fibres are traced downwards, because the bulk of both pyramidal tracts becomes diminished from above downwards. The degeneration occurs simultaneously throughout the whole length of the fibres, and is only " **descending** " in the sense that it occurs **below** the site of the lesion, the trophic nerve-cells of the neurons being at upper ends of these in the brain.

If the interference with the descending tracts be in the cord, there will be degeneration below the lesion, but only to a very slight extent above it.

Secondary ascending degeneration may occur from pressure on, or injuries to, the cord, or from transverse or other form of myelitis, etc. The posterior columns and the direct cerebellar and the antero-lateral (Gower's) tracts will be affected throughout their whole extent in the cord—the other tracts, if they suffer by the injury, in the various regions

in which they are situated. Thus, in the lumbar and lower dorsal regions, the whole of the ascending columns will be degenerated; but, on passing upwards, the degeneration becomes limited to the postero-internal columns and the direct cerebellar tracts.

PELLAGRA : In practically all cases of this epidemic disease there is sclerosis in the posterior columns, and, usually, in the lateral pyramidal tracts. There is also atrophy of the nerve-cells of the anterior horns of the grey matter (fig. 458).

The degeneration of the nerve-cells is very extensive,

FIG. 465.—*Ascending Degeneration in the Postero internal (Goll's) Column.* The result of pressure by a tumour on the lumbar part of the cord. (Pal-Weigert Method.) ×6.

nucleus is pushed to one side and the rest of the cell shews marked chromatolysis.

TUMOURS OF THE CORD are rare. Gliomas may occur, starting especially in the tissue around the central canal. Myxomas and sarcomas have been observed. Cystic conditions have already been discussed. Secondary involvement of the cord by tumours of the membranes or of the bony walls of the canal: or by tumours which have invaded and eroded these bony walls, is common.

PARASITES : *Echinococcus-cysts* and *Cysticercus cellulosæ* may occur, but are exceedingly rare. Trypanosomes are found in the cerebro-spinal fluid in cases of sleeping sickness.

DISEASES OF THE PERIPHERAL NERVES AND GANGLIA

NEURITIS.—Under this term are included both **inflammatory** and **degenerative** changes, and it is not possible, for purposes of description, to separate the two conditions absolutely, as true inflammatory changes may lead to those of a degenerative nature.

The causes of the condition are grouped as follows :--

1. **NEURITIS OF TRAUMATIC ORIGIN.**—The damage may be the result of gunshot or other wounds of the nerves, of pressure by tumours.

Fig. 466.—*Longitudinal Section of a Degenerating Nerve.* Shewing the fragmentation of the myelin. (Stain, osmic acid.) × 200.

aneurisms, or foreign bodies, or by narrowing of the foramina through which they pass, *e. g.* in cases of syphilis, tuberculosis, etc. In other cases, the nerves become implicated in scar-tissue. The changes which take place in the peripheral nerves after injury vary with the severity of the injury, and the degree of destruction. If the continuity of a nerve is severed, secondary degeneration occurs throughout the entire peripheral part, which has been cut off from its trophic nerve-cells. The myelin breaks up into droplets and eventually, by the aid of the phagocytic cells derived from the proliferated neurilemma-cells, is absorbed; and the axis-cylinders disintegrate. In addition, many observers have found certain minor grades of degeneration in the central end of the nerve, extending up to the neuron-body.

Following the **degeneration,** if the continuity of the parts be preserved, and in favourable circumstances, there may occur repair or

regeneration—complete or incomplete, as the case may be. As to the method by which regeneration is brought about, there is still some uncertainty, different views being held as to whether the repair starts from the distal end of the central or upper portion, or from the proximal end of the peripheral part. For convenience, we shall speak of the former as the " central " and the latter as the " peripheral " end of the divided or injured nerve. It is generally agreed that the proliferated cells of the sheath of Schwann, however derived, become closely arranged in long, tubular strands.

According to those who accept the **central hypothesis,** the reparative process starts from the cut end of the proximal or central portion of the severed nerve. The original nerve-fibres, they maintain, either grow downwards into the peripheral segment; or a number of young axis-cylinders are formed by division of each original axis-cylinder at the first node of Ranvier above the point of injury. These young axis-cylinders grow downwards into the original neurilemma-sheaths; or fresh neurilemma-sheaths may be formed from the proliferated neurilemma-nuclei.

The second or **peripheral hypothesis** was advanced in 1891, but, at that time, it was not seriously entertained by most neurologists. In spite of this, several workers on the subject, including Kennedy, Ballance, and Purves Stewart, have strongly supported it. Stated very briefly, the view which they maintain is that the peripheral segment of a divided nerve degenerates completely. This degeneration begins in a few hours after the injury, and is nearly complete in from three to four weeks. In the old sheath, the proliferated cells, which are arranged in regular columns, act as **neuroblasts** or nerve-formative cells. Close to the nucleus of the neuroblast, a young, somewhat wavy axis-cylinder is developed, which soon becomes separated from the nucleus. Round this axis-cylinder, a delicate myelin-sheath is formed, the remaining neuroblasts forming the new neurilemma-sheath. The young axis-cylinders join end to end to form more or less continuous chains, but do not undergo full development until they have become united to the central end of the nerve. These observers further state that the existing axis-cylinders at the central end play an entirely passive part, until they become joined to the new peripherally-formed fibres.

Fleming,[1] who supports this peripheral hypothesis, maintains, however, that, in addition, new axis-cylinders are formed, at the central end of the divided nerve, from the old axis-cylinders. It seems probable that regeneration may take place by both methods.

The **regeneration after section** is brought about in the same way as that following on degeneration; but the newly-formed cells and the developing axis-cylinders —being no longer guided by the remnant of

[1] R. A. Fleming, " The Peripheral Theory of Nerve Regeneration with Special Reference to Peripheral Neuritis," *The Scottish Medical and Surgical Journal,* September 1902, p. 193.

the original sheath—may take a tortuous course, especially if the two ends of the nerve are widely apart. If a temporary " scaffold " or guide, e. g. strands of catgut, be placed between the ends, the regeneration is more rapid, and the course taken by the regenerating fibres is more direct.

2. **NEURITIS OF TOXIC ORIGIN.**—This group includes most of the cases of **multiple neuritis** following infective diseases, e. g. diphtheria, typhoid and scarlet fevers, etc.: those caused by such substances as alcohol, carbonic oxide, carbon bisulphide, phosphorus, and the metallic poisons—lead, mercury, zinc, copper, etc.: and those occurring

FIG. 467.—*Transverse Section of a Nerve from a case of Myxœdema.* Shewing myxomatous areas in the connective tissue. There are also patches of degenerative change in the nerve-fibrils themselves. (Van Gieson's stain.) ×60.

in such diseases as diabetes, acute and other forms of rheumatism, Bright's disease, etc. Most of these last-mentioned instances are due probably to toxic substances—the result of bacterial infection, or of disordered metabolism.

The neuritis of beri-beri, which some authors regard as infective in origin, is generally regarded as a result of disordered metabolism due to vitamine-deficiency. Rose Bradford and his fellow-workers have recently described a filter-passing organism which they claim to have isolated from cases of multiple neuritis, and with which they believe that they have produced experimentally, in animals, multiple neuritis. This condition described by them must be regarded as a **primary** neuritis due to toxins produced within the body by a specific organism. It begins usually with more or less severe constitutional symptoms, and might well be classed as **acute infective polyneuritis.** Their observations, however, need further confirmation.

In these toxic cases, the nerve-trunks become swollen and of a reddish colour, and there may be very extensive degenerative changes, producing wide-spread paralysis, as is seen sometimes in cases of diphtheria. In such cases, and probably also in those due to lead-poisoning, changes occur both in the nerve-endings in the muscle and in the muscle itself. In the nerves, all degrees of degeneration, from simple swelling of the medullary substance to complete destruction of the whole structure, may occur. Usually, there is proliferation of the neurilemma nuclei. In cases due to diphtheria, the nerve-sheaths, the blood-vessels, and the lymph-spaces, are sometimes the seat of inflammatory changes, and the degeneration of the nerve-fibres may go on side by side with the inflammatory reactions.

In **alcoholic neuritis,** the process is generally subacute. The changes vary considerably, and paralysis, in some cases, occurs without much evidence of degeneration. The axis-cylinder is affected early, but, in addition, there is proliferation of the connective-tissue cells of the endoneurium, perineurium, and epineurium. The blood-vessels are dilated, and leucocyte-infiltration may be a prominent feature. The nerves of the legs are, in most cases, first affected, and may be the only ones involved. Similar changes are seen in **Raynaud's disease** and in **beri-beri.** In the latter condition, the nerves of the lower limbs are specially liable to become involved, but the pneumogastric, the phrenic, and the vasomotor nerves of the face, are not infrequently affected. The most constant lesion, however, is in the muscles. The fibres are diminished in size, have a homogeneous appearance, and shew proliferation of their nuclei, with, in addition, a considerable increase in the supporting fibrous tissue.

In the **neuritis due to mineral poisons,** the axis-cylinders persist for a long time, but degeneration of the medullary sheaths takes place—it may be over only short lengths of the nerve, e. g. involving one or more internodes of Ranvier. Very commonly, there are associated changes in the nerve-cells of the anterior horns; and, in certain cases, e. g. in lead- and in arsenic-poisoning, a thickening of the connective-tissue septa of the nerves and a leucocytic infiltration take place. In **lead-poisoning,** the motor fibres are more affected than the sensory, the nerves of the forearms and hands being specially involved, producing the characteristic " wrist-drop." The nerves of the larynx are occasionally affected. Oculo-motor paralysis occurs, and optic nerve-atrophy is not infrequent. In **arsenic-poisoning,** the nerves of the legs are usually first affected.

In the **neuritis of diabetes, Bright's disease, etc.,** a purely degenerative condition, without any evidence of inflammation, takes place; and changes of the nature of arterio-sclerosis are generally found in the small blood-vessels, and may be responsible for the nerve-changes. Degenerations are found in the posterior columns of the cord, and in the cells of the anterior horns. The degeneration begins by the breaking-up of the myelin into short segments, and the change is confined largely to

the medullary sheath. Only a few fibres in a bundle may be affected. The axis-cylinders become beaded or varicose, but well-preserved. Degenerative changes, usually myxomatous in type, are found in nerves in some cases of myxœdema.

3. **NEURITIS DUE TO THE LOCAL ACTION OF AN ORGANISM,** e. g. the neuritis produced by leprosy, in which disease *B. lepræ* is present primarily in the nerve-trunks. In the **neuritis of leprosy,** the nerve-lesion is confined almost exclusively, at least in the earlier period of the disease, to the connective-tissue sheaths of the nerves, these sheaths undergoing considerable proliferation. In the cellular proliferations, *B. lepræ* is found in enormous numbers. The changes in the nerves are secondary and degenerative in type.

TUMOURS[1] :—

Neuromas.—**True neuromas** are tumours formed by the actual proliferation of the axis-cylinders, as well as of the accompanying fibrous tissue. The proliferated fibres are non-medullated, and form a very complex mass which, on section, is found to be composed of true nervous tissue. **False neuromas** are usually **fibromas** or **myxomas,** which have developed from the connective tissue in or around nerves. In these, there is no actual neoplastic overgrowth of the nervous-tissue elements proper; but the connective tissue may penetrate between the nerve-fibres and split the nerve up into distinct bundles. The structure of the nerve-fibres which pass through the tumour, is usually unaltered, but partial or complete disappearance of the myelin-sheath may occur.

After section of nerves, e. g. in amputations or in wounds, the distal end of the central portion of the divided nerve may become swollen and simulate a tumour. On careful examination, it is seen that the new formation is composed of granulation-tissue, in which there is a **limited** amount of proliferation of true nervous tissue. These so-called "**amputation neuromas**" are thus, in the great majority of cases, really the result of an attempt at repair, and are not true tumours; although, in very rare instances, neoplastic growth supervenes upon the reparative processes. Such "neuromas" consist of bundles of nerve-fibrils embedded in an overgrowth of developing fibrous tissue derived from the endoneurium and perineurium.

Ganglion-neuromata have been described as occurring in the mesentery, the adrenals, and elsewhere. The tissue of the tumours contains nerve-cells and nerve-fibres. Those found in the adrenals are very malignant and are composed mainly of tissue resembling undifferentiated sympathetic neuroblast—and have been called **neuroblastomas.** The general view is that they are **embryomas** in which the neuroblastic tissue predominates.

In **Neuro-fibromatosis (von Recklinghausen's disease**—*see* p. 287), multiple nodules appear on the peripheral nerves and are associated with subcutaneous swellings. In these nodules, individual nerve-fibres are found interspersed among the fibrous tissue.

[1] See also under **Neuroma,** p. 301.

DISEASES OF THE BONES AND JOINTS

Bone consists of a dense matrix arranged in layers—the lamellæ—impregnated with lime-salts, chiefly phosphate, and containing irregularly-shaped branching cells (bone-corpuscles), enclosed in lacunæ, from which run branching canaliculi. The bony tissue may be either **compact** or **spongy** in character. In the spongy bone, the blood-vessels run in the interstices, supported by the marrow; but, in compact bone, they are contained in the Haversian canals, round which the lamellæ are arranged in a concentric fashion.

Immediately under the periosteum, the bone is denser than at other parts, the lamellæ here being pierced by canals for blood-vessels which join those in the Haversian canals. The periosteum is composed of two layers, the inner of which is highly vascular and contains numerous **osteoblasts** or bone-forming cells.

Bone is formed by an **ossification in connective tissue,** and may or may not be preceded by the formation of cartilage. In the **ossification of cartilage,** the cells become enlarged and arranged in definite rows; and, in the matrix, as well as in, and around, the cartilage-cells, granules of calcareous matter are deposited. At the same time, the osteoblasts at the deeper part of the periosteum form fibrous lamellæ, in which they themselves become enclosed to form **bone-corpuscles.** Later, the lamellæ become calcified. This sub-periosteal layer of bone extends inwards, the calcified cartilage being absorbed by it, and irregular spaces—the medullary spaces—are formed, which become filled with **osteoblasts.** These osteoblasts, in their turn, produce new lamellæ, which become calcified. The absorption of the calcified matrix appears to be effected by large multinucleated cells—the **osteoclasts.** The regular lamellæ are not laid down till some time after birth.

At a later period, the cartilage, at one, or more usually at both, ends of the long bones, begins to ossify from a separate centre or centres. Normally, these **epiphyses** do not become joined to the shaft by ossification of the epiphyseal cartilages until the growth of the bone is completed. The bones increase in length in virtue of a growth of the cartilage which intervenes between the shaft and the epiphyses, and a gradual extension of the ossification into it. They grow in width by successive deposits of fresh bony layers under the periosteum, and, therefore, in operations in which bone is removed, it is important, if possible, to injure the osteogenetic layer of the periosteum and the epiphyseal cartilages as little as possible. Some authors regard this osteo-genetic layer as belonging to the bone rather than to the periosteum, but, in our references, in the succeeding pages, to the formation of new bone, we shall assume that this layer is **periosteal.** It is probable that, in the growth of bone, the balance between the osteoblastic and the osteoclastic processes is influenced by some **internal** secretion. This may explain, in part, the imperfect development in rickets and in cretinism. The overgrowth in acromegaly is associated with disease of the pituitary body; and extirpation of the parathyroids in the rat is said to be followed by a diminution of the
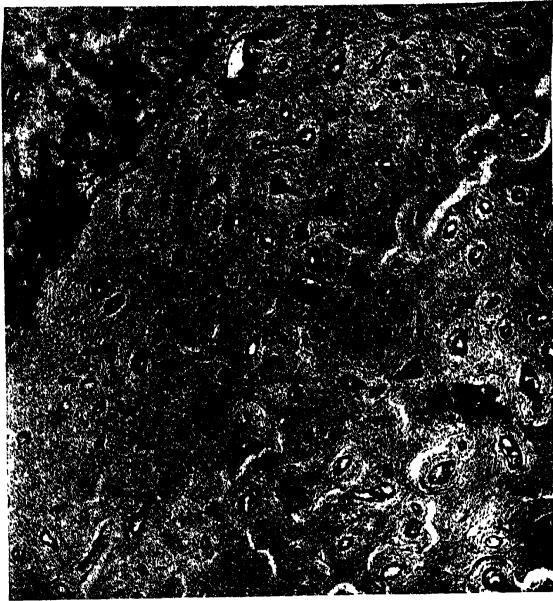
FIG. 468.—*Transverse Section through Normal Compact Bone (Tibia)*. Shewing the Haversian Canals, round which may also be seen the concentric lamellæ. Periosteum is shewn at upper left corner. (Lent by Professor Alexis Thomson, C.M.G.)   ×28.
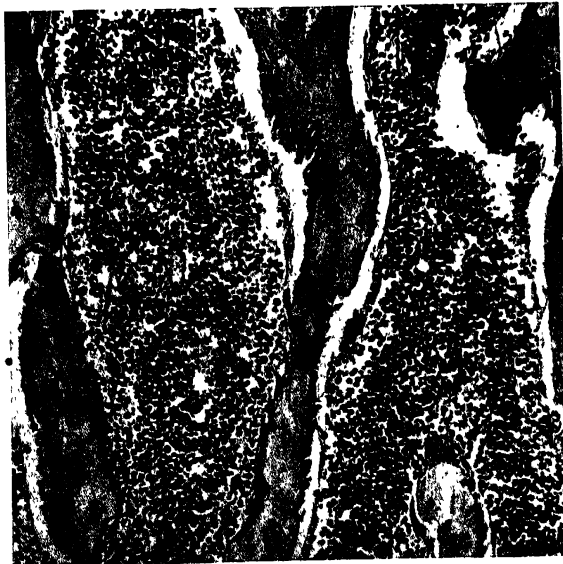

FIG. 469.—*Longitudinal Section of the Upper End of the Tibia of an Infant.* Shewing spicules of newly-developed compact bone, with layer of osteoblasts on their surface; and cellular bone-marrow in the intervening spaces of the bone. The white spaces are due to artificial retraction. (Lent by Professor Alexis Thomson, C.M.G.)   ×100.

calcium-content in the blood and a defective deposition of lime in the bones. **Calcification** and **ossification** of cartilage may take place prematurely, and lead to a certain impairment of movement. This early calcification is frequently seen in the costal cartilages. In some cases, this is associated with a defective blood-supply, resulting from arterial degeneration.

In **intra-membranous ossification,** the lime-salts are deposited in a fibrous tissue which contains numerous osteoblasts.

In studying the diseases of bone, it should be remembered that the formative activity of this tissue is retained more completely and efficiently than that of practically any other structure in the body : that the bones are constructed upon a definite plan which enables them to resist the various mechanical forces, of necessity applied to them : and that, therefore, plastic overgrowth, guided by a definite architectural design, may take place under the influence of various stimuli.

Thus, where fracture or bending of bones has occurred, there may be overgrowth of osseous tissue for protective purposes; but, in addition, there is a definite plan of reconstruction in order to meet the new lines along which pressure or stress may be applied to the injured bones.

MALFÓRMATIONS OF BONE.—A premature coalescence (**Synostosis**) of the bones, or of component parts of a bone, may occur, and lead to various deformities. Among the commonest of these malformations are **synostosis of the sacro-iliac articulation,** which leads to narrowing of the pelvis, either on one side, or on both sides, depending upon whether there is affection of one or both articulations; and **synostosis of the epiphyseal cartilages** in growing bones, which may bring about " shortening "—or, more accurately, deficient growth and elongation — and other abnormalities in the long bones. The condition of premature synostosis of the cranial bones, said to occur in microcephaly, has already been described (*see* p. 965). There may also be abnormal **osseous union** between the bones of the tarsus or carpus, and, associated with this or distinct from it, **absence** of certain of the bones. Such malformations may be symmetrical on the two sides.

Absence of bones such as the clavicle, the lower jaw, the patella certain bones of the skull, etc., may be a congenital condition. Deficiency in the neural arches is seen in cases of **spina bifida** (*see* p. 992). **Excessive and irregular growth of bone** may be seen in **gigantism** and in **acromegaly** (*see* pp. 857 *et seq.*).

Other malformations of bones occur, but are not of sufficient pathological importance to call for description.

RICKETS.—This disease is limited to childhood, and, usually to the first two years of infancy, developing usually between the seventh and eighteenth months of extra-uterine life.

Ætiology.—Though the essential cause of rickets is still obscure, there seems to be little doubt that it is, to a large extent, connected in some way with **improper feeding** and **bad hygienic surroundings.** It is

extremely common among the poorer classes. It has been pointed out, however, that the disease often occurs in children who have been weakened by some acute disease, such as measles or scarlet fever; and it seems probable that improper feeding and absence of fresh air and sunlight may act in the same way, by weakening the individual, and thus interfering with the normal ossification of the bones. Experiments on animals have shewn that, if the diet is deficient in "vitamines," the bones are fragile and easily break off at the junction of the shaft and epiphysis. The jaws are brittle and the teeth usually loose. There are marked swellings on the ribs at the bone-cartilage junction. Hæmorrhages into the tissues, such as are seen in scurvy, were marked in these experimental animals. Various chemical hypotheses have been propounded to explain the development of the disease—such as a deficiency of phosphorus or of lime-salts : or an excess of lactic acid, which, being a solvent of lime-salts, has been supposed to prevent their deposition in the bones. None of these hypotheses is supported by facts. Another possible explanation is that the primary cause of the condition is an auto-intoxication originating in the alimentary canal, and, in favour of such a view, is the constant presence of gastro-intestinal disturbances in these cases.

Some authorities have held that rickets is merely a manifestation of congenital syphilis, but, though syphilis may, and often does, occur along with rickets, there is, we think, no doubt that the two conditions are entirely independent, and that rickets may occur in children in whom congenital syphilis is, in the highest degree, improbable.

Morbid Anatomy.—Rickets produces deformities, not only in the **shape** of the bones, but also in their **structural characteristics.** These changes are due partly to **absorption,** and partly to **irregular** but **excessive growth.**

They manifest themselves in the following ways :—

(1) **Enlargement** of the ends of the long bones, especially at and near the cartilaginous zone between the ossifying epiphyses and shaft.

(2) **Softening** of all the bones.

(3) **Thickening** of the flat bones, e. g. the scapula, the pelvis, and the skull.

(4) **Deformities** of the softened bones, produced usually by mechanical means.

Enlargement of the ends of the long bones is seen best at the junction of the ribs with the costal cartilages—the so-called "beading of the ribs"—and at the lower ends of the radius, ulna and tibia, but may occur in any of the long bones. The enlargement is due to an **excessive formation of the structures which precede ossification,** to an **irregularity in the method of** bone-formation, and to **a retardation of the process.** There is an abnormal increase in the amount of spongy tissue; the bone, in which the irregular ossification is taking place, is much more vascular than normal; and reddish, vascular areas may also be seen in the cartilage.

The **blue line of cartilage** which marks the junction of the epiphysis with the shaft of the bone is usually very irregular, considerably thickened, and in marked contrast with the uniform, well-defined narrow line seen in normal ossification.

On microscopical examination, there is a considerable increase in the breadth of the zone of multiplying cartilage-cells. The cells are in much larger numbers, and are arranged in rows which are much more irregular than those seen in normal ossifying tissue. The individual cells may be swollen, or may be smaller than normal—such variation in size being a marked feature of the condition. Calcification of the matrix;
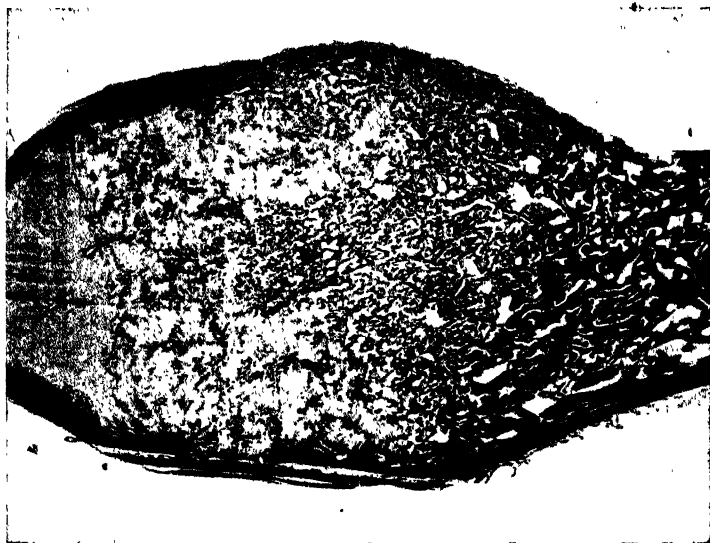
FIG. 470.—*Longitudinal Section of Costo-Chondral Junction.* From a case of Rickets, shewing a very broad and irregular line of ossification. (Lent by Professor Alexis Thomson, C.M.G.) × 5.

and of the cartilage-cells, is also irregular, some of the calcified cells lying close to the line of ossification, others being situated at considerable distances from it. Sometimes, the cytoplasm of the cartilage-cells calcifies, whilst the nucleus remains unaltered. This irregular calcification of the cells may take place close to, and be continuous with, the bone, the uncalcified nucleus resembling a bone-corpuscle, and suggesting the possible transformation of cartilage-cells into bone-corpuscles. Blood-vessels are seen in the midst of the cartilage, having penetrated from the bone—hyaline cartilage being, under normal circumstances, a non-vascular tissue—and, around the vessels, **absorption** and **ossification** may be taking place simultaneously. In the **osteogenetic** layer of the periosteum, an excessive formation of cells and an increased vascularity occur, and the osteoblasts may form a layer of considerable thickness. Bone may

Fig. 471.—*Longitudinal Section of a Costo-Chondral Junction.* From a case of Rickets, shewing the irregular zone of ossification at the line of junction between cartilage and bone. (Lent by Professor Alexis Thomson, C.M.G.) ×4.

Fig. 472.—*Longitudinal Section through a Costo-Chondral Junction.* From a case of Rickets, shewing the swelling and irregular ossification at junction of bone and cartilage. (Lent by Professor Alexis Thomson, C.M.G.) ×5.

be formed in excessive amount, but is usually very spongy in character, imperfectly developed, and, as a general rule, very vascular. The matrix is granular, the lime-salts being deposited in an irregular fashion, and true bone is not formed. Thus, the condition is rather one of calcification than of ossification, and the new tissue has been described as " **osteoid** " tissue. The flat bones may become thickened. As a result of this pathological ossification, the bones may be enlarged, but the enlargement consists of soft, spongy tissue which is not able to resist pressure or traction, and, in consequence, deformities of various kinds arise.

Fig. 473.—*Longitudinal Section of a Costo-Chondral Junction.* From a case of Rickets, shewing irregular areas of cartilage (to the right) and very irregular masses (dark) of " osteoid " tissue. × 30.

Deformities of the Bones due to Rickets.—Thickening or " clubbing " of the growing ends of the bones is a common feature, which may persist in later life, though, in many cases, it ultimately disappears. The bones are usually short and thick, but, during the active course of the disease, they bend easily and give rise to various deformities, which may become permanent when the soft rickety bones become denser and firmer, as they do when the active period of the disease passes off.

In the **long** bones, the deformities due to mechanical agencies occur especially in the lower limbs, and take the form of curvatures, the two principal forms of which are **Genu valgum** and **Genu varum**.

In **Genu valgum**, or **knock-knee**, there is usually a curving of the lower part of the femur—the **convexity** of the curve being **inwards**. Thus, the internal condyles of the femora are thrown together, and are placed

Fig. 474.—*Extreme Rickety Deformities of the Femur and the Tibia.* (These were the bones of David Ritchie, Scott's "Black Dwarf.") Note the flattening of the shafts of the deformed bones. (Edinburgh University Anatomical Museum. Catalogue No., Os. D. i. 8.)

at a lower level than the external ones. The tibiæ diverge from one another, but are not necessarily curved. The femur may, in addition, shew an anterior curvature, and the tibia a similar condition. In an advanced stage of the deformity, the knee-joints may cross each other.

In **Genu varum,** or **bow-legs,** the shafts of both the femora and the tibiæ are curved—the **convexity** of the curve being **outwards.** The tibia·

usually shews the condition in much more marked degree than the femur. Anterior curvature may also be present.

Marked deformities in the bones' of the arms are not so common. **Partial or complete fracture** of the long bones is—on account of their softness—liable to occur in the earlier stage of the disease. In such an incomplete or **" greenstick-fracture,"** the convex surface of the bone gives way, but the concave does not.

In the **chest,** the deformity may be very marked, and its effects serious. Besides the " beaded " appearance of the ribs, to which reference has already been made, there may be, during inspiration, and while the bones are still soft and yielding, a drawing in of the ribs, and the production of a depression which runs transversely from the lower end of the sternum across the chest, on each side, to the posterior margin of the axilla, about the level of the diaphragm. Another depression is produced which runs obliquely down the anterior aspect of the chest on each side, along the line of junction of the bony ribs with the costal cartilages. It is in the line of this latter depression that

Fig. 475.—*Rickety Deformities of Tibia and Fibula.* Note the flattening of the bones—especially of the Fibula—and the sickle-shaped margin. (Edinburgh University Anatomical Museum. Catalogue No., Os. D. i. 23.)

the " beading " of the ribs is seen. These changes cause a straightening of the ribs, with a consequent pushing forward and bending of the sternum **(pigeon-breast appearance).** The deformities thus produced may greatly interfere with the respiratory movements, and, in cases in which other diseases supervene, may seriously complicate them.

The softening of the **vertebræ** leads to the occurrence of curvature, which may be merely an exaggeration of the normal antero-posterior curvature **(kyphosis** and **lordosis).** Lateral curvature **(scoliosis)** also frequently occurs. The spinal curvatures tend to produce corresponding

deformities of the thorax and abdomen, and displacements and other abnormalities in their contents. The chief deformity in the **pelvis** is a pushing forward of the sacrum, and a consequent diminution in the antero-posterior diameter of the inlet—a condition usually associated with lordosis or exaggeration of the lumbar convexity. In the **skull,** the bones may be thickened, the circumference of the cranium increased, and the summit flattened, so that the frontal eminences bulge, and, in severe cases, the forehead may overhang the face. The parietal eminences may also be very prominent, and produce—along with the protuberant frontal bones—the square or box-shaped cranium. The closure of the fontanelles is usually delayed. Occasionally, especially in the occipital region, areas of the cranial bones may be very thin and atrophied, and can be easily indented by pressure with the finger. This condition, which is called **Craniotabes,** is a common manifestation of congenital syphilis, and it is doubtful if it occurs in rickets uncomplicated by that disease.

In · rickets, **recovery** from the active disease very commonly takes place, but, usually, a varying degree of deformity, persists. A reparative process frequently supervenes, and a definite **sickle-shaped ridge** (*see* fig. 475) is produced along the concavity of the shafts of the deformed long bones. This acts as a kind of buttress, and may considerably strengthen the bones, which, in after life, not infrequently become abnormally dense in character. It is common to find, in association with rickets, enlargement of the liver, dilatation of the stomach, enlargement of mediastinal glands, gastro-enteritis, etc.

SCURVY-RICKETS (INFANTILE SCURVY—BARLOW'S DISEASE):—
This is really a scorbutic manifestation in a rickety child.

Hæmorrhagic extravasations are common, and are found in the sub-periosteal tissues in the tibia and femur near the joints. Occasionally, the epiphysis becomes separated. Hæmorrhages in the gums and from the mouth, nose, bowel and kidney may occur. The periosteum of the affected bone becomes thickened and unduly vascular, and the underlying bone rarefied. New sub-periosteal bone may be formed, but this is always imperfect.

ACHONDROPLASIA.—In this congenital disease, the ætiology of which is not known, the growth of those bones which are formed in cartilage, is deficient. The **epiphyses** of the **long bones** are enlarged, but the **diaphyses** "shortened," *i. e.* there is deficient elongation. The **frontal region of the skull** is unduly prominent, and the **base** is proportionately diminutive. The **mandible** is usually prominent and the bridge of the nose depressed.

Microscopically, the bones present many of the features of rickets,— the rows of cartilage-cells in the epiphyseal line are irregular, and the cells are enlarged and shew very little evidence of proliferation.

ATROPHY OF BONE :—

True atrophy of bone is seen commonly in old age, and consists of a general diminution of the organic matrix, with an increased porosity, and a decrease in thickness, of the bone. This **senile atrophy** is well seen in the lower jaw (*see* fig. 476), in the bones of the skull, and both in the shaft and at the articular ends of the long bones—the neck of the femur often shewing the change in an extreme degree, with alteration in its angle, predisposing to fracture.

Atrophy from disease is seen in the bones of the limb above the seat of an amputation (*see* fig. 477), or in a limb which, from paralysis or as a result of fracture or other injury, is not used. The atrophy **associated with various nervous lesions** is probably, in part, an atrophy due to disuse, and thus the atrophy seen in infantile paralysis, in pseudo-hypertrophic paralysis, and in locomotor ataxia, may be partly explained. The nervous mechanism, however, has an important rôle in such cases, and, in some, *e. g.* in the atrophy following leprosy, the involvement of the nerves in the leprous lesion, with the consequent loss of their trophic influence, must be regarded—apart from the actual invasion of the bones by the infective process itself—as the main causal factor in producing the wasting of the bone.

Atrophy due to pressure is illustrated in the erosion of bony structures such as the sternum or the vertebræ by aneurisms (*see* fig. 265, p. 559), tumours, etc., and the erosion of the skull by the Pacchionian bodies. The process, in these cases, is, however, rather one of absorption than of true atrophy. •　　　　•

The important and profound changes which occur in the bones in connection with the various **reactions of the bone-marrow as a hæmo-poietic tissue,** have already been discussed in the Chapter on **Blood Diseases,** p. 586.

OSTEOMALACIA is especially a disease of women, generally commencing during pregnancy, and gradually increasing during the whole period of child-bearing. It is relatively more common among the poor and ill-nourished; and unduly frequent child-bearing seems to play some part in its causation. In its early stages, it affects especially the bones of the pelvis, but, later, the disease may spread to the vertebræ, the ribs, and the femora. The bones of the head, and those of the hands and feet, are implicated only in very exceptional cases. The affected bones are so soft that they can be readily cut with a knife; and bending of them, wherever pressure is exerted, is a common result. In the pelvis (*see* fig. 478), the bones become compressed or pushed inwards at the acetabula—*i. e.* in the lines of pressure which pass through the heads of the femora—as well as at the sacrum, through which the weight of the

FIG. 476.—*Atrophy of the Lower Jaw in Old Age.* The bone is greatly reduced in size, edentulous, and with its alveolar border completely absorbed. (Edinburgh University Anatomical Museum. Catalogue No., Os. D. b. 2.)

FIG. 477.—(A.) *Atrophy of Head and Upper Part of Shaft of Humerus* following upon amputation. (B.) *Head of opposite Bone for comparison.* (Specimens lent by Mr. Henry Wade, C.M.G., D.S.O.)

body is communicated. The symphysis pubis is pushed forward, making a beak-like projection; and the anterior surface of the sacrum shews an increased concavity, its promontory being carried forward. The cavity of the pelvis is thus narrowed, and the pelvic inlet becomes markedly heart-shaped or tri-radiate. From the nature of these distortions, the pelvis has been termed the **crushed** or **beaked pelvis.** The femora, and perhaps the other long bones of the lower limbs, may shew marked bending; and, if the vertebræ are softened, there may be curvature and twisting of the spine in various directions. The ribs soften, and so-

FIG. 478.—" *Crushed Pelvis.*" From a case of Osteomalacia.

called "spontaneous" fracture occurs, the lateral diameter of the chest being narrowed and its antero-posterior diameter increased.

Changes in the affected bones.—There is a decalcification of the bony trabeculæ near the medullary spaces and the Haversian canals—this process gradually extending towards the surface. Associated with the decalcification, absorption and atrophy of the trabeculæ occur, and, thus, the medullary spaces are increased in size. These changes are usually very irregularly distributed. The decalcification commences at the surfaces of the trabeculæ, often leaving the central part ossified.

In the advanced condition, there may be merely a thin external layer of bone, surrounding very spongy tissue, in which calcareous salts

may be left only in very few areas. The bone-marrow shews usually a great increase in all its cellular elements, the large osteoclasts or multi-nucleated giant-cells being specially abundant; and hæmorrhages are not uncommon.·

Stefanelli and Levi (*Riv. crit. di clin. med.*, August 1908) reported the isolation of a diplococcus from two cases of osteomalacia, and the repro-duction of the disease in a mild form in rats which had been inoculated with this organism by Morpurgo—nine out of thirteen animals being affected. This work has not been confirmed, and the view commonly
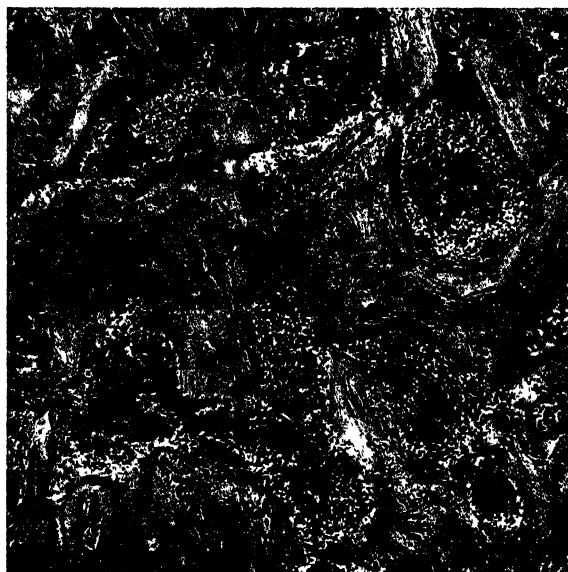
Fig. 479.—*Section of a Vertebral Body in Osteomalacia.* Shewing widening of the medullary spaces, with absorption of the bony trabeculæ. ×60.

held at present is that the disease is due to some pathological modifica-tion of the internal secretion from some of the genital organs.

Forms of deformity of bones associated with chronic nephritis have been described as *osteomalacia* by several authors. In these cases, the bones are soft and can readily be cut with a penknife, and the changes have been marked especially at the neck of the femur and the lower end of the radius or tibia, the bending of the bones being very marked. Infantilism is frequently an associated condition.

CIRCULATORY DISTURBANCES IN BONE :—

Venous congestion and **thrombosis** may occur in bones as in other tissues and organs.

Hæmorrhage, either under the periosteum or into the bone-marrow,

may result from traumatism, or be a manifestation of osteomalacia, of scorbutus, or of purpura. The effused blood may cause separation of the periosteum from the bone, and so bring about necrosis. Extensive hæmorrhage into the bone-marrow may also occur in acute infective conditions, e. g. streptococcal septicæmia.[1]

INFLAMMATION OF BONE : OSTITIS or OSTEITIS, PERIOSTITIS, OSTEOMYELITIS :—

- The majority of cases of inflammation in bone occurs in childhood, when the tissue is still actively growing. The inflammation is very often suppurative in character and due to pyogenetic organisms, either introduced directly by a wound, or carried by the blood-stream from some more or less distant infective focus, such as skin, tonsils, etc., to the bone and lodged there, possibly, in many cases, at an injured focus. In later life, inflammation of bone may be secondary to **bullet or other wounds,** to septic infection spreading from the site of **amputations,** or to a **compound fracture** of any bone. In all these cases, the organisms are introduced from without at the time of the injury—they are of the pyogenetic type and the inflammation is usually **suppurative** in character.

Abscesses form at, and in the neighbourhood of, the seat of injury, and may invade the medullary cavity, destroying the bone-marrow. **Thrombosis** of the veins is a frequent sequel, and, owing to disintegration of the septic thrombus, **pyæmic abscesses** may be produced, especially in the lungs and the wall of the heart. The injury may be a slight one, but the fact that the inflammation occurs most commonly in bones which are exposed to external violence, and that boys are more frequently attacked than girls, points to injury as having an important relationship to the disease. Though various pyogenetic bacteria may be the cause of such acute suppurative conditions in bone, *Staphylococcus pyogenes aureus* is the organism most commonly found, the term **staphylococcal fever** being sometimes applied to such cases. Any cause of general or local lowering of resistance, such as cold or one of the exanthemata, is a predisposing factor.

Typhoid osteitis is a well-recognised condition occurring during or after an attack of typhoid fever, and is of the nature of a subacute or chronic periosteomyelitis, most commonly in the tibia, but not infrequently in the ribs and sternum.

The characters of the lesions vary considerably, depending upon the virulence of the organism, the seat of infection, and the resisting power of the patient—such suppurative conditions of bone being most frequent in weakly children. The bones most commonly affected are the long bones, especially the tibiæ; but the vertebræ, the ribs, and the bones of

· · [1] Carnegie Dickson, *The Bone-Marrow*, Longmans, Green & Co., London, 1908, p. 140.

the pelvis, may also be attacked. In a long bone, the primary lesion is usually para-epiphyseal, *i. e.* in the shaft on the diaphyseal side of the epiphyseal cartilage, but may commence in the epiphysis itself. The bone-marrow is affected very early, and the inflammatory reaction spreads along the para-epiphyseal line and under the periosteum. Pus forms, fills the medullary cavity, invades the looser sub-periosteal tissue, and spreads to the bone itself. The 'spread to the neighbouring joint is usually arrested by the epiphyseal cartilage.

In some cases, especially the **periosteum** is involved (**acute periostitis**), and shews all the phenomena of acute inflammation and suppuration. The pus accumulates between the periosteum and the bone, and the latter, being thus separated from its main source of blood-supply, may undergo **necrosis.** In the majority of cases, the inflammation and suppuration tend to be more widely spread, and to involve the periosteum (**periostitis**), the bone (**ostitis** or **osteitis**) and the medulla (**osteomyelitis**); and pus may be present in the substance of the bone and in the medullary cavity. Necrosis of bone is common in these cases, and, as just noted, is due to an interference with the blood-supply, as well as to the local action of the bacteria and their products (*vide* **Necrosis of Bone,** pp. 1034–6).

Localised abscesses may be found in bone, especially in the cancellous tissue at the extremities of the long bones, usually in close proximity to the epiphyseal cartilage, *e. g.* in the head of the tibia, on the diaphyseal side of the cartilage (Brodie's abscess, etc.). These may be due to a primary infective condition of the bone itself; or may arise during an attack of typhoid fever, scarlet fever, measles, etc. These abscesses become surrounded by a dense wall of bone.

CHRONIC OSTITIS may be a sequel of necrosis of bone (*see* p. 1036), the dead portion keeping up the irritation; or it may result from traumatic causes, round foreign bodies such as bullets, and round fractures, especially where union is delayed, or from specific, slowly-acting irritants such as those of tuberculosis and syphilis. The changes produced may be either of a **formative** or of a **rarefying** type.

In the **formative** type, there is thickening of the bones, especially from new formation on the surface, the deeper layer of the periosteum proliferating and giving rise to a species of granulation-tissue, the cells

Fig. 480.—*Necrosis of Bone.* Shewing sequestrum (pale) in centre, surrounded by the "new case." (R. C. S. Museum, Edinburgh.)

acting as **osteoblasts.** This new formation may also take place in the medullary canal, and the bone may become greatly thickened and condensed.

In the **rarefying** type, the granulation-tissue cells act as **osteoclasts,** and bring about absorption of the bony trabeculæ, thus widening the various spaces and channels—a condition which is seen especially in the shafts of the long bones. Usually, side by side with the rarefying process, there is also new formation taking place, so that, though the bones may become more cancellous, they may, at the same time, be increased in thickness.
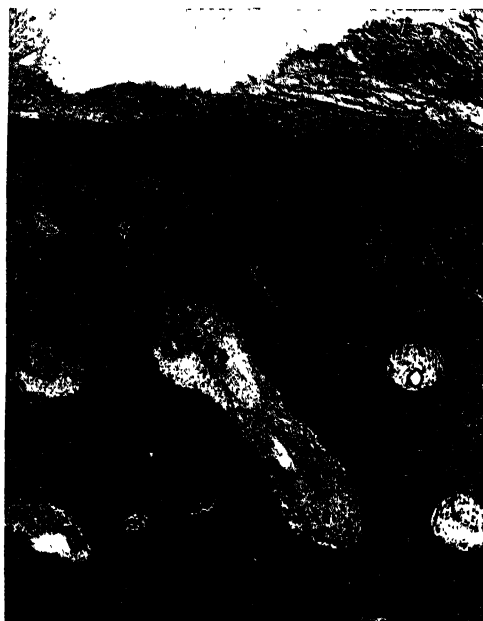
FIG. 481.—*Sclerosis of Phalanx.* Shewing thickening of periosteum and increased density of the subjacent bone formed from it, together with narrowing of medullary spaces. (Lent by Professor Alexis Thomson, C.M.G.)   ×45.

CARIES OF BONE :—

Caries is a term applied to the softening and destruction of bone, and is seen especially in tuberculous affections, but may also result from osteomyelitis, and be frequently associated with necrosis. The bone is extremely **soft** and **spongy,** and breaks down readily. Further reference will be made to this condition under **Tuberculosis of Bone** (p. 1041).

NECROSIS OF BONE.—In **necrosis,** there is death of a portion of bone, this being brought about principally by the **separation of the periosteum from the bone by non-suppurative or suppurative inflammatory exudates,** etc., and the consequent **cutting off of the principal**

source of blood-supply. It may develop also as a result of acute or chronic inflammatory changes in the bone itself, and is extremely common in connection with bullet- and other wounds and injuries, sequestra, in such cases, being frequently multiple when much splintering of the bone has occurred.

Morbid Anatomy.—The necrosis may be localised, or may involve an extensive portion, or even the whole shaft, of a long bone, an epiphysis, or even some of the flat bones, e.g. the skull. The **dead piece of bone** sometimes retains its form and general appearance, but it frequently·

Fig. 482.—*An Osteophyte,* in which the bone is undergoing absorption by osteoclasts lying adjacent to the bony trabeculæ. (Lent by Professor Alexis Thomson, C.M.G.) ×60.

becomes white, opaque, dry, and very hard. With the necrosis, there are always associated inflammatory conditions, in the relation either of cause or of effect; and the dead bone **(sequestrum)** becomes surrounded by a mass of granulation-tissue, in which ossification may take place. Thus an irregular external **new case** or shell surrounding the dead bone may be produced (*see* fig. 483); and, in this, the sinuses through which the pus is discharged remain as permanent apertures. This new bone is, at first, soft and friable, but, later, becomes thick and dense, forming the **involucrum,** or case; and, eventually, it is strong enough to act as the shaft of the bone. A varying degree of absorption of the sequestrum may take place, and sequestra of small size are frequently discharged through a sinus. If the sequestrum is large, it may remain in position for years.

Phosphorus-Necrosis.—This condition, which occurs among phosphorus-workers, is supposed to be due to the local action of the vapour of yellow-phosphorus. The condition begins in the periosteum—a great formation of new cancellous bone taking place on the surface of the upper jaw. Bacteria enter from the mouth, by way of carious teeth, and, after a time, the inflammation becomes suppurative, with the result that separation of the periosteum, and necrosis, which may involve the whole upper jaw, take place. The lower jaw may also be involved, and the sequestrum, which forms as a result of the necrosis, separates very slowly. It has been stated by several observers that this condition of " phossy-jaw," as it has been called, is, in reality, due to the presence of *B. tuberculosis*—the poisonous action of the phosphorus preparing the way for, and perhaps also acting in conjunction with, this organism. The disease is now extremely uncommon, on account of the substitution of amorphous phosphorus for the yellow variety in the manufacture of matches, and we have not personally had the opportunity of testing the relationship of tuberculosis to the necrosis.

HYPERPLASIA AND HYPERTROPHY OF BONE :—

In studying these conditions, a very noticeable feature is the great formative power which bone possesses. In almost no other structure ot the body is such perfect repair carried out; and in no other is there such a power of reversion to a more primitive type of structure. The formation of new bone, " callus," is thus a common

Fig. 483.—*Necrosis of Bone.* Around the Sequestrum the " new case " has been formed. From a patient with chronic osteomyelitis. (Edinburgh University Anatomical Museum. Catalogue No., Os. D. d. 38.)

phenomenon, and this formative capacity is not confined to the periosteum, but is also exhibited by the tissues in the cancellous spaces, medullary cavity, and Haversian canals, *i. e.* osteoblasts and marrow-tissue, blood-vessels, lymphatics, nerves, etc. The new bone may thus

arise from the periosteum, or from structures in the medullary canal, and also from the cancellous and Haversian spaces within the substance of the bone itself; and the ossification may spread to the surrounding parts, and often occurs in excess. In this excessive growth of bone, marked deviations from the normal sometimes take place and new lines of support may form in the architecture of the bone.

*Ætiology.—The causes of this excessive growth of bone may be divided into those which are **reparative** in their nature: those which are truly **hyperplastic** and caused by various local or general irritants: and those which are **neoplastic.**

(a) **REPARATIVE OVERGROWTH** has been referred to under the **formative type of chronic ostitis** (pp. 1033–4), and will be again discussed in connection with the **repair of fractures** (p. 1039).

(b) **HYPERPLASTIC OVERGROWTH.**—It is impossible definitely to separate some forms of hyperplastic overgrowth from those which are produced during the processes of repair. As a result of chronic irritation, there may be a true hyperplasia; but the mode of production of the new bone is essentially the same as that which occurs in the process of repair. Thus, in the local formation of new bone in the region of chronic ulcers, or round a piece of necrosed bone, the new formation cannot be distinguished from the bone which is produced in the filling up of the cavity from which the necrosed portion has been removed. A more general hyperplasia is seen in syphilis and in mercury-poisoning. In the latter condition, the thickening of the bone is liable to occur especially in young animals, and may be due to an interference with the normal absorption and modelling, rather than to an actual stimulative overgrowth.

Overgrowth, essentially different in its causation from that occurring in repair, may take place in certain situations, and may be confined to certain bones. Thus, in the condition of **Acromegaly** (q. v., p. 858), there are enlargement and thickening of the bones of the fingers and toes, of the bones of the lower jaw, the maxillary part of the upper jaw, and the malar, nasal, and frontal bones; and, not unusually, there is thickening of the bones of the pelvis, together with minor alterations of a similar nature in the sternum, clavicles, ribs, vertebræ, and other bones.

Local overgrowth of bone may occur at the sites of attachment of muscles on which there is special strain. These overgrowths constitute the so-called **osteophytes** (see p. 1046, " diaphysial aclasis ")—the best example of this condition being furnished by the so-called " rider's bone " at the lower attachment of the adductor magnus; such osteophytes are not uncommon in cases which have previously suffered from rickets.

(c) **NEOPLASTIC OVERGROWTH.**—Definite bony tumours will be described later (p. 1045).

(d) **OSTEITIS DEFORMANS (Paget's Disease of Bone).**—In this condition, there is enlargement, with general thickening, of some of the bones, especially of the tibiæ, the clavicles, and the bones of the cranium. The bones are very spongy, and, though greatly thickened, are much lighter than normal in weight. The surface presents a finely-pitted appearance. In the long bones, the articular ends are much enlarged, the medullary cavity is narrowed; and, in the lower limbs, the bones are usually bowed forwards and outwards. At first, the changes are often more marked in one bone than, in others, and, usually, the bones of the hands and feet, shew no similar pathological changes. In the skull, there may be very great thickening, with obliteration of the diploë. The head may shew enormous enlargement, which may be asymmetrical, the temporal fossæ become shallow, and the forehead prominent and overhanging. The facial bones are generally unaffected, and no marked narrowing of the foramina occurs. The dorsal and lower cervical spine may shew a marked degree of kyphosis, the ribs are thickened and their curvature increased, but the pelvis is usually only slightly affected, though, in rare cases, a condition resembling osteomalacia has been described as occurring in it. Arterial degeneration is frequently associated with this condition, and, in some cases, atrophy, of the thyroid and suprarenal glands has been noted.

FIG. 484.—*Paget's Disease* (Osteitis Deformans). The tibiæ are curved throughout their whole length, with the convexity of the curve directed forwards. The circumference of the shaft is uniformly increased from end to end. (Edinburgh University Anatomical Museum. Catalogue Nos., Os. D. k. 5 and 6.)

On **microscopical examination,** there is marked rarefaction from absorption of bone, with widening and increased formation of Haversian canals.

REPAIR OF FRACTURES :—

When a bone is fractured, there is generally some laceration of the periosteum, and, it may be, of the surrounding tissues, with resulting **hæmorrhage.** There may be, and usually is, some **displacement.** Repair is brought about by the same series of reactions as occur in the healing in an incised wound in a connective tissue, with, in addition, the special processes of bone-formation; and the repair may, in the same way, be delayed, or even prevented, by lack of apposition of the fragments, by movement, and by the presence of torn tissues such as muscle, or of excess of effused blood, between the broken ends of the bone, or by septic processes. In repair, the **vessels** in the bone, in the medullary cavity, and in the periosteum, **become dilated.** There is **transudation of lymph** with **emigration of leucocytes.** If apposition of the fragments is maintained, these reactions may last for from one to six days.

On the second or third day after the injury, the periosteum shews active cellular proliferation, especially in its deeper part; and there is also proliferation of the endothelial cells of the blood-vessels. This proliferative change extends for some distance beyond the seat of fracture, and it also invades the periosteum, separating its different layers. Similar proliferative changes are seen in the bone itself, and in the marrow. Young blood-vessels, arising from pre-existing vessels, pass into this cellular tissue, and any effused blood undergoes absorption. Thus, masses, more or less extensive, of vascular granulation-tissue, are formed.

This granulation-tissue—many of the cells of which are multinucleated and correspond with osteoclasts, whilst others are of the nature of osteoblasts—may become fibrous or cartilaginous; but, usually, in the human subject, definite ossification takes place in its deeper layers, the new bone being formed in trabeculæ continuous with the outer layers of the original bone. Contemporaneously with this new formation of bone, absorption and modelling go on. The changes, in fact, are exactly analogous to those seen in normal ossification. By the successive deposit of new layers, a large ensheathing mass of **callus** may be produced. In the interior of the bone, and between the fractured ends if there is displacement, similar masses of callus are produced. The **internal callus** may almost completely fill the medullary canal; whilst the **intermediate callus**—especially if apposition has been maintained—is usually small in amount, and is probably in part derived from the tissues in the Haversian canals, and in part by an extension both from the **external and internal callus.**

The **provisional callus,** thus formed, undergoes absorption by osteoclasts, new layers of bone possessing definite Haversian systems are laid down, and these are arranged so that they are adapted to the exact line of strain—the internal architecture of the bone often becoming greatly modified, especially if the union has taken place with the ends of the bones out of position.

FIG. 485.—*Fracture of the Leg of a Mouse* (12 days). Shewing the masses of ensheathing and intermediate callus. The fractured ends of the shaft of the femur (*a* and *b*) of are displaced. (Lent by Professor Alexis Thomson, C.M.G.) ×15.
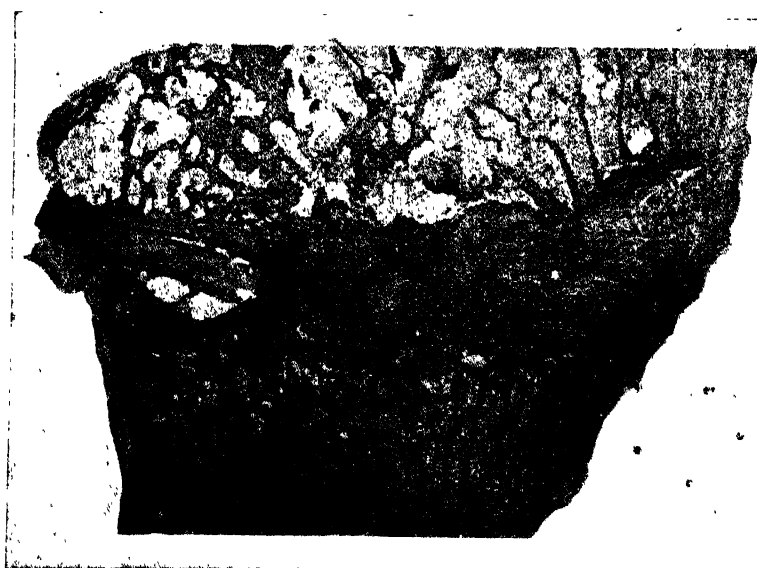
FIG. 486.—*Horizontal Fracture of the Internal Malleolus* (three weeks). Shewing a zone of intermediate callus. (Lent by Professor Alexis Thomson, C.M.G.) ×4.

Sometimes, and especially if the parts have not been kept sufficiently at rest, the proportion of fibrous tissue in the callus is greater than that of normal bone, and, in this way, imperfect union by fibrous tissue may take place. In like manner, a species of false joint may be formed, furnished, perhaps, with a cavity and with smooth articulating surfaces covered with fibrous tissue.

· **TUBERCULOSIS OF BONE** is extremely common, and may produce very serious pathological changes. The infecting virus—*B. tuberculosis*, commonly of the bovine type—is carried by the blood-vessels or by the lymphatics, and becomes lodged either in the periosteum or in the bone. Spread may also occur secondarily from affected joints; but, very

FIG. 487.—*Tuberculosis of the Os Magnum*. Showing cellular proliferation, with tubercle-follicles (left, lower part), caseation, and absorption of bone. (Lent by Professor Alexis Thomson, C.M.G.) ×28.

frequently, the bone adjoining the articulation is first affected. Cellular proliferation takes place at the seat of lodgment of the bacilli, and definite tubercle-nodules are produced. These nodules show giant-celled systems, and, as these increase in size and undergo caseation, the bony trabeculæ become gradually absorbed. **Necrosis** frequently occurs, the necrosed portion becoming separated, and lying in a cavity which has softened, caseous walls. The necrosed portions (sequestra) may be very small; but they may be large and rarefied where the lesion is an acute infiltrating one : or dense and sclerotic where the necrosis has taken place because of interference with the circulation.

Caries is a more frequent result of the tuberculous process, large areas of bone becoming irregularly softened and eroded, so that cavities lined by

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tuberculous granulation-tissue may be produced. The caries may lead to collapse of the affected bones, for example the bodies of the vertebræ in Pott's disease of the spine (*see* fig. 463). Frequently, a process of necrotic softening resembling suppuration develops—the so-called **cold abscess**—the contents consisting of caseous débris, pus-corpuscles, etc. This condition is best seen in **lumbar or psoas-abscesses**. The tuberculous process may infect the periosteum either primarily or secondarily, and, if there is extensive infiltration, sub-periosteal abscesses form, with necrosis of the underlying bone. The cancellous tissue is the favourite nidus for the commencement of the process; but the earliest change may be seen occasionally in the midst of dense bone; whilst the periosteum, in certain cases, is the

Fig. 488.—*Caries of the Head of the Tibia and Articular Surface of the Patella.* From a case of tuberculosis. (Sheffield University Pathological Museum.)

starting-point of the affection. It is not uncommon to find tuberculosis more or less extensive in the bone-marrow, which may also be affected as part of a general miliary tuberculosis (*see* pp. 614, 616 and 619). The bones most commonly attacked are those rich in cancellous tissue, *e. g.* the vertebræ, the bones of the hands and feet, and the extremities of the long bones. The bones of the skull are not often involved, but tuberculosis of the temporal bone may occur secondarily to tuberculous disease of the middle ear; or tuberculosis may implicate some of the bones at the base of the skull where the affection has spread upwards from the vertebral column.

The tuberculous process is accompanied by the ordinary phenomena of chronic inflammation, as well as by rarefaction, so that the surface of the bone is usually rough and shews irregular projections, the result of a formative periostitis. It is not uncommon, however, to find a tuberculous sinus surrounded by very **dense** bone.

Healing of the tuberculous area may take place, the caseous material being absorbed and replaced by granulation-tissue, and, later, by fibrous tissue, which may undergo calcification or ossification.

SYPHILIS OF BONE :—

The lesions affecting the bones in cases of late secondary and of tertiary syphilis usually have their seat in the periosteum, and are of the nature of a **gummatous periostitis.** During the more acute stage, there may be considerable proliferation of the cells of the periosteum, and the formation of irregular **periosteal nodes.** As the **gummata** increase in size, the central parts become caseous, and the bone underneath shews an irregular eroded surface. In some cases, e. g. in the bones of the skull, this erosion is extreme, and necrosis, with the formation of sequestra, with a "worm-eaten" appearance, may be produced, and perforation perhaps supervene. The sequestra, in some cases, remain partially separated for years. The gummata sometimes undergo softening, and actual abscess-formation may arise. After the gummatous nodes disappear, sub-periosteal thickening, with erosion, and even perforation—which is seen especially in the cranial bones and in the palate—may remain. Associated with the nodes, there are always changes which are referable to chronic inflammation—the medullary canal becomes narrowed or even filled up, and sub-periosteal thickening of the bone is a common feature. Thus, the bones may become much thicker, denser, and heavier than normal.

Fig. 489.—*Tibiæ exhibiting Syphilitic Nodes on their Shafts.* (Edinburgh University Anatomical Museum. Catalogue No., Os. D. e. 4 and 10.)

The bones specially affected by syphilis are the tibia, the ulna, the parietal, occipital, and frontal bones, the clavicle, the sternum, and the ribs. The epiphysis of a bone is sometimes affected and involvement of the joint may result.

In certain cases, syphilitic disease of a mucous membrane may spread to the bones and cartilages, and cause erosion and perforation. This condition is seen especially in the bones of the palate and of the nose.

In the long bones, sub-periosteal infiltration may lead to caries; and gummata which are sometimes found in the cancellous tissue, either in the epiphysis or at the end of the diaphysis, may remain latent for a long time or may lead to a definite syphilitic osteomyelitis, with erosion of the inner compact layers of bone and even " spontaneous " fracture. An osteomyelitis of the phalanges (**syphilitic dactylitis**) is not uncommon in children congenitally infected.

In **congenital syphilis,** the bones of the skull may become, at parts, thinned and softened, and the condition of **craniotabes** be produced (*see* p. 1027). In the long bones, the cartilage-cells in the ossifying area may undergo marked proliferation, and be associated with irregular calcification of the matrix; and, beneath this ossifying area, there is sometimes an excessive formation of granulation-tissue or even of soft, fluid or semi-fluid, pus-like material. Separation of the epiphysis may occur as a result of the process. A definite **syphilitic epiphysitis** may occur in early infancy, especially in the bones of the knee and in the head of the humerus, but other epiphyses may be involved and several are often affected simultaneously.

ACTINOMYCOSIS, and the closely-allied condition, **MYCETOMA,** may occur in bone, generally as a result of extension from adjacent parts. A periostitis is first produced, but, gradually, there develops caries, which, at first, is superficial, but, later, involves considerable areas of bone.

LEPROSY may give rise to osteomyelitis and periostitis, but, in most cases, it produces caries and necrosis, especially of the phalanges.

CURVATURES OF THE SPINE :—
These need be referred to only very briefly.

1. **Antero-posterior Curvature :—**

(*a*) **Angular Curvature,** so-called, is due to a local tuberculosis of the bodies of the vertebræ. The eroded bodies are not able to support the weight of the body upon them and consequently give way, producing a more or less pronounced angle, the spinous processes becoming unduly prominent behind. The spinal cord is not necessarily injured, but, frequently, it is compressed, and the conducting fibres are interrupted (*see* fig. 463). In some cases, it may become involved by a direct spread of the tuberculous process.

(*b*) **Kyphosis.**—In this condition, there is a marked convexity of the spine backwards, generally most marked in the dorsal region. In its less pronounced forms, it is due chiefly to muscular weakness, to emphysema or to the habit of stooping. Kyphosis is almost always present in cases of **acromegaly;** and, in its most exaggerated forms, is usually due to **rickets.**

(c) **Lordosis** is usually confined to the lumbar region, where it constitutes an exaggeration of the normal lumbar convexity. It is generally a manifestation of rickets, though it may also occur in congenital dislocation, and in ankylosis, of the hip. The convexity of the curve is forwards.

2. Lateral or Rotato-lateral Curvature : Scoliosis :—

In this condition, there is a lateral deviation, with a partial rotation of the vertebræ. This may develop in rickets; or, in its milder forms, it may merely be the result of a bad habit in standing or sitting. Lateral curvature, of necessity, produces corresponding deformities of the chest and shoulder-girdle, and also of the abdomen and pelvis, together with displacements and other abnormalities of internal organs. One of its most serious results is extensive collapse of the lung.

TUMOURS OF BONE :—

SIMPLE TUMOURS.—**Fibromas** may develop from the periosteum, and, in them, spicules of bone are sometimes found. **Chondromas** may grow in the substance of the bones—producing expansion of them—or in the periosteum; or they may arise from the cartilages—most usually from epiphyseal cartilages or from displaced fragments of these—at the ends of the bones. They appear to be of most frequent occurrence in rickety subjects, and are usually multiple (see fig. 490). They often shew **myxomatous degeneration,** which

FIG. 490.—*Chondroma growing from bones of Hand.* (Edinburgh University Anatomical Museum. Catalogue No., Os. D. p. 6.)

produces marked localised softening, and even the formation of cyst-like cavities—the so-called " **cystic** " **chondroma.** In some instances, they undergo more or less imperfect **ossification.**

Osteomas may occur as **exostoses** or as **enostoses**. The **exostoses** are formed generally in fibrous tissue or in cartilage. They are frequently multiple, and may be symmetrical. They have been divided into

the **ivory** exostoses, when composed of very dense bone, and **spongy** exostoses, when of cancellous bone. Some are formed from cartilage, and, in these, a layer of cartilage covers the ossifying tumour as long as it is growing. The spongy exostoses are found especially in connection with scats of attachment of muscles—the ivory ones being commoner on the bones of the skull. The **enostoses** are bony tumours which arise in the **interior** of the bone. Keith [1] maintains that the multiple exostoses are really due to a disorder of growth, and are not true tumours. He adopts the name, suggested by Morley Roberts for this condition—" **diaphysial aclasis.**" In this disease, the normal "modelling process,"
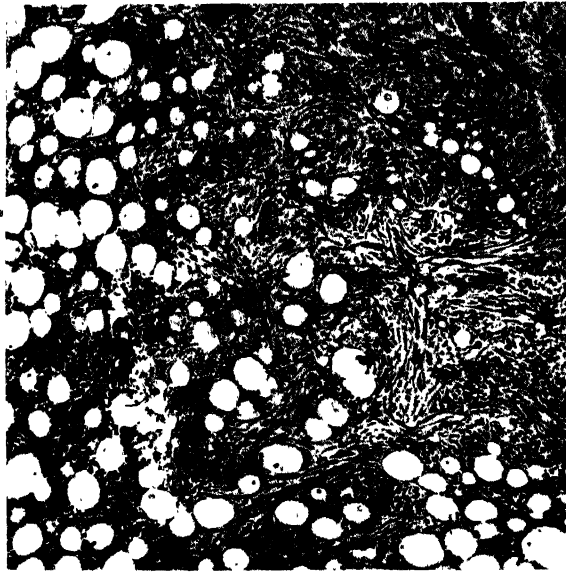
Fɪɢ. 491.—*Mixed-celled Sarcoma of Head of Tibia*, invading the bone-marrow. × 75.

is arrested, and, between the properly formed part of the shaft and epiphyseal end of the long bones, there is interposed an irregular cylinder of imperfectly modelled bone, on the surface of which there are, usually, several outgrowths. "Diaphysial aclasis " is, according to this view, primarily a disturbance of growth-discs, and of both the cartilaginous and periosteal elements comprised within these discs.

Myxomas, Lipomas and **Angiomas** occur, but are rare.

Myelomas, which are generally classed as sarcomas (myeloid sarcomas), are moderately common. They are usually localised, and shew comparatively little tendency to give rise to secondary deposits in the viscera or in lymphatic glands. They are found especially in the upper

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[1] Keith—Report of Medical Society of London—*Brit. Med. Jour.*, December 27, 1919, p. 847.

FIG. 492.—*Myeloma of Shaft of Femur.* Macerated and dried specimen, shewing expanded shell of bone.
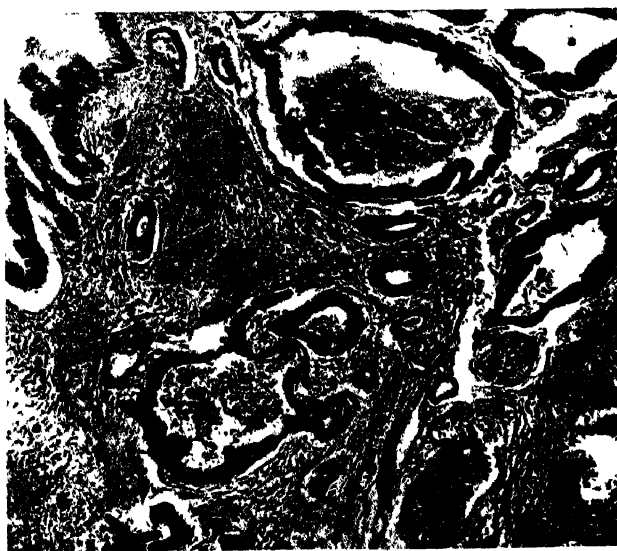
FIG. 493.—*Malignant Adenoma, secondary in the Rib.* (Primary growth in stomach.) × 75.

and the lower jaws, and in the cancellous tissue at the articular ends of the long bones. They may be round-celled, spindle-celled, etc.; and, in their growth, they sometimes cause considerable destruction of bone, which may become eroded or expanded (*see* fig. 492), and, as a result, so-called " spontaneous " fracture is very liable to occur.

MALIGNANT TUMOURS.—Sarcomas are the commonest form of malignant tumour of bone. They may be primary or secondary, and may grow from the periosteum or from the medulla. Those growing from the periosteum may be **round-celled, spindle-celled** or **mixed-celled,** and the tissue of which they are composed is liable to undergo imperfect ossification. Sometimes, this tendency is very marked, and the term **osteosarcoma** is applied to the tumours in which it is found.

Secondary sarcomas in bone, apart from those of melanotic type, are rare.

Secondary cancers are very frequent, and any type may occur. The bones may, indeed, shew very wide-spread metastases in cases of gastro-intestinal, mammary, and other forms of cancer, such cases usually presenting a profound degree of anæmia from destruction of the bone-marrow. In scirrhus and other malignant tumours of the breast, secondary growths are extremely frequent in the bodies of the dorsal and lumbar vertebræ, a matter of great importance to the surgeon from the point of view of prognosis in such cases. Occasionally, such implication of the bone-marrow in cancer is so extensive that almost no part of the osseous skeleton escapes, the term **diffuse carcinomatosis of bone** being applied to the condition.

PARASITES :—

Hydatids of bone occur, and may be of the " exogenous " variety.

DISEASES OF JOINTS

MALFORMATIONS :—

DISLOCATIONS and DEFORMITIES of joints may be **congenital** or **acquired.** Among the most important of these are **congenital dislocation of the hip**—in which the head of the femur generally lies on the dorsum of the ilium above and behind the acetabulum, which is usually deficient—and the various forms of **club-foot (talipes varus, valgus, equinus,** and **calcaneus,** or combinations of these). **knock-knee (genu valgum), bow-legs (genu varum),** and **flat-foot**—for full descriptions of which reference should be made to surgical textbooks.

In some of the forms of **talipes,** the deformity is congenital in origin; in others it is due to paralysis of certain muscles, the remaining (unpara-lysed) muscles pulling upon the foot and bringing about the deformity. In **·talipes varus,** the evertors of the foot are paralysed, the foot being inverted, and its inner margin raised upwards by the unopposed **tibialis anticus** and **posticus.** In **talipes valgus,** with paralysis of the inverting muscles, the foot is turned outwards, the outer border is raised, and the heel is usually drawn up from the unopposed action of the **peronei, the extensor longus digitorum,** and the **gastrocnemius** muscles. In **talipes equinus,** due to paralysis of the anterior muscles of the leg, the muscles of the calf are contracted, and, in consequence, the tendo Achillis and heel are raised and the foot extended. In **talipes calcaneus,** where the calf-muscles are paralysed, the heel is depressed, and the foot is flexed at the ankle, the contracted muscles being the **tibialis posticus,** the **peronei,** and the **extensors.** Certain **combinations** of these deformities are of more frequent occurrence than the above-mentioned simple forms, **talipes equino-varus** being by far the commonest variety of club-foot.

INJURIES.—These may give rise to lacerations of the synovial membrane, hæmorrhagic extravasations, suppuration, tearing of ligaments, displacements of cartilages, dislocations, fractures, etc., but, for full descriptions of these, reference should be made to works on Surgery.

INFLAMMATORY, DEGENERATIVE, and **PROLIFERATIVE CHANGES in JOINTS :—**

(a) **SIMPLE** or **NON-SUPPURATIVE ARTHRITIS.**—In this condition, the synovial membrane is congested, and it and the articular cartilages become covered with a fibrinous exudate, the cavity being occupied by a clear or slightly turbid and viscid serous fluid, which may considerably distend it. At·this stage—that usually seen in **acute rheumatism**—the disease may resolve, and the joint return to its normal condition, suppuration practically never supervening in **uncomplicated**

acute rheumatic arthritis. In certain other types, however, especially if the joint has become infected by a perforating or an open wound, or during an operation, the inflammation may go on to **suppuration.** The synovial membrane becomes thickened, infiltrated with inflammatory cells, and converted into granulation-tissue. The condition may spread to the cartilage—this becoming softened and ulcerated—to the periosteum, and to the bone. Even in this advanced stage, the inflammation may subside; but there is usually left great rigidity, and even ankylosis of the joint. The union may become fibrous or osseous in nature.

In **rheumatic arthritis,** one of the writers has noted **irregular areas of congestion in the synovial membranes,** and from these areas a *Streptococcus* has been isolated, which has produced arthritis when inoculated intravenously into rabbits.[1] A non-suppurative arthritis may occur in cases of **pneumonia** and of **epidemic cerebro-spinal meningitis,** due probably to toxins; and an analogous condition is not uncommon after **injections of anti-sera,** etc.

The joints may become involved by spread from a neighbouring osteomyelitis, epiphysitis, bursitis, or cellulitis. Even the joint-affections due to the ordinary pyogenetic streptococci and staphylococci, are not, in all cases, necessarily suppurative. More usually, however, unless in the very early stages, these forms of arthritis are purulent.

(b) **PURULENT ARTHRITIS.**—This may be due to the secondary infection of a primarily non-suppurative arthritis with pyogenetic bacteria; or it may be a purulent condition from the first. Thus, **in wounds** and **in pyæmia,** there may be an acute infection of the joints, with very rapid suppuration, and the whole joint-cavity may become distended with pus. Similarly, in diphtheria, scarlet fever, typhoid and paratyphoid fevers, pneumonia, epidemic cerebro-spinal meningitis, meningitis due to "leptothrix" or other organisms, etc., a purulent arthritis may occur; though, as has been stated above, these diseases may, in some cases, give rise to a non-suppurative form. The synovial membrane becomes converted into suppurating granulation-tissue, and that part of the latter which overlaps the edges of the articular cartilages assists in their erosion. Eventually, these cartilages undergo necrosis and absorption, the ends of the bones show rarefying osteitis, the periosteum is inflamed and, later, new bone may be thrown out and osteophytic projections developed.

(c) **GONORRHŒAL ARTHRITIS.**—In this condition, there may be accumulation of turbid serous fluid, or even of pus, in the joint, and, within the cells of the exudate, the *Gonococcus* or *Micrococcus gonorrhœœ* may be found. More commonly, however, the inflammatory reaction resembles that seen in acute articular rheumatism, and the character-

[1] J. M. Beattie, " Experimental Work in Relation to *Micrococcus rheumaticus* and *Streptococcus pyogenes,*" *Jour. Med. Research,* January 1906, **vol. ix.,** No. 2, pp. 399–421.

istic organism may be found in the exudate only after prolonged search. The larger joints are more commonly affected than the smaller ones— the knee-joints being involved in about seventy per cent. of the cases, and the ankle in about twenty-five per cent.

(d) **GOUTY ARTHRITIS.**—In this condition, the urate of sodium is deposited, generally in the form of acicular crystals, in the tissues of, and also in those surrounding, the joint. At first, the deposit takes place in the cartilages, especially towards the surface: and, later, in the synovial membranes, the ligaments, the bones, and the soft tissues round the affected joints. Some authors regard a primary degeneration of the cartilage and cartilage-cells as an essential preliminary to the deposit of the urates within them.

The crystals cause considerable irritation, and produce acute, sub-acute, and chronic inflammatory conditions. Suppuration never occurs in uncomplicated gout. The joints most frequently involved are the small articulations of the hands and feet. (See p. 69).

(e) **CHRONIC RHEUMATIC and RHEUMATOID ARTHRITIS (Osteo-arthritis, Arthritis Deformans).**— The changes in the joints in these two conditions are very similar, and some authorities look upon them as identical. Until more information is obtained as to the causal agent, the classification of these chronic joint affections must remain in a very unsatisfactory position. Poynton and Paine describe a condition simulat-ing chronic rheumatic arthritis occurring in a rabbit which had received an intra-venous injection of a streptococcus isolated from a case of acute rheumatism; and one of the authors has produced, by intra-venous injection, and also by direct injection of a similar organism into the knee-joint, chronic arthritis with proliferative overgrowth and ulceration of cartilage. These experiments seem to point to the relation of some forms of the disease to acute rheumatism, a fact borne out by clinical experience in the human subject; but **true rheumatoid arthritis** has not been pro-duced experimentally, and there is, apparently, as yet very little clinical evidence that it is in any way related to acute rheumatism.

(i) In **Chronic Rheumatic Arthritis,** i. e. the chronic form of arthritis, which is a sequel of, or allied to, **acute rheumatism,** the changes are very similar to those found in rheumatoid arthritis, but they are not usually so extensive.

(ii) **Rheumatoid Arthritis** occurs especially in women, and affects first the smaller joints of the hands and feet. The wrists, knees, and ankles may be affected comparatively early; and, later, the vertebral and temporo-maxillary joints may become involved. In the early stages, the changes appear particularly in the **synovial membranes,** which shew an increased vascularity, and become somewhat thickened. There is, usually, excess of synovial fluid. The **synovial fringes** enlarge, and **papilliform project-ions** are formed at the margins of the joints. These are produced by a proliferation of connective tissue covered by serous membrane, and, in

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them, cartilaginous nodules may form. Fat is sometimes deposited in the fringes, to a very considerable degree. Some of these projecting masses occasionally become detached, and form "**loose bodies**" in the

FIG. 494.—*Chronic Rheumatoid Arthritis.* Showing proliferated synovial fringes and projecting papilliform bodies: "lipping" of the articular margins: and invasion of the cartilage over the inner condyle of the femur by the proliferated synovial fringes. (Edinburgh University Anatomical Museum. Catalogue No., Os. E. g. 32.)

joint-cavity   Calcification or ossification may occur in these fringes, though these changes are commoner in osteo-arthritis.

The **articular cartilage** becomes softened—especially at those parts along the surfaces of contact—and assumes a fibrillated or velvety appear-

ance. At a later stage, erosion takes place, the articular surfaces being at parts rubbed away by friction; at the same time, proliferation of the cartilage may cause it to extend beyond its normal limits; and, if this overlapping cartilage becomes calcified or ossified, considerable deformity ("lipping," etc.) of the articular surfaces may be produced. The cartilage becomes somewhat translucent. Though the **articular ends of the bones** may, for a considerable period, shew little pathological alteration, there may be exten-
sive softening of the bones, and, in some cases, enlargement. The surface, where deprived of its cartilage, may become smooth and polished—**eburnation** (*see* fig. 495). Associated with the changes which have been described, there is often considerable thickening of the ligaments and other fibrous structures round the joints, great muscular wasting, and marked impairment of the movements of the joints. There may be ankylosis.

Organisms (bacilli, strepto-cocci, staphylococci, etc.), which have been regarded as causal, have been isolated, by various observers, from cases of chronic rheumatoid arthritis, and chronic rheumatic arthritis. One of the authors (W. E. C. D.), in a large number of cases of chronic rheumatic arthritis (and from cases clinically in-distinguishable from chronic

Fig. 495.—*Chronic Rheumatoid Arthritis.* The articular ends of the tibia and femur, shewing eburnation of the surface of the internal tuberosity and the internal con-dyle, with antero-posterior grooving. The articular surfaces also shew lipping. (Edin-burgh University Anatomical Museum. Catalogue No., Os. E. g. 37.)

rheumatoid arthritis) has isolated streptococci, from the urine, and com-paratively small doses of vaccines prepared from these organisms have produced intense reactions in the affected joints. Such cases, very frequently, had some septic focus in which streptococci predominated or were even the only organisms present. He considers that this—in addition to the amelioration of the joint-condition under such treat-ment, and on the removal of such septic foci in the teeth, tonsils, nasal sinuses or elsewhere—is evidence of the possible causal relationship between the streptococci and these forms of chronic joint-affection.

STILL'S DISEASE.—In this condition, there is stiffness and fusiform

swelling of the joints, due mainly to synovial and peri-articular thickening. The cartilages may become pitted and eroded, but the bones are not usually affected, and ankylosis does not occur. The disease, which may closely resemble rheumatoid arthritis, commences usually before the age of the second dentition, and is characterised especially by hard, painless enlargement of the lymphatic glands, and, frequently, by splenic hyperplasia. Muscular atrophy is a marked feature round the affected joints—knees, ankles, wrists and neck. Numerous joints may become successively involved. The condition is generally regarded as a chronic **infective arthritis.**

SENILE ARTHRITIS.—This form of **Osteo-arthritis,** which is regarded, by some authors as an extreme degree of rheumatoid arthritis, occurs especially in the hip-joint. The articular cartilage becomes softened and lustreless, and its matrix fibrillated. Erosion of the cartilages takes place, and this, combined with an associated proliferation at their edges, gives rise eventually to the formation of osteophytes. The head of the femur becomes enlarged. The proliferative outgrowth at the articular margins may be very considerable, producing an irregular ring, or everted lip, of bone encircling the head. A similar projection of bone may occur at the margin of the acetabulum; and, in this way, very great impairment of movement may be produced. The head of the bone becomes worn away, sometimes to an extreme degree, and the surface may become polished and enamel-like at the areas of contact at which the bones grind against one another (**eburnation**). The cancellous bone may become attenuated and absorbed. Bony ankylosis does not occur. The synovial membrane may shew villous overgrowth and considerable fatty invasion. In this condition, there is no exudation into the joint-cavity.

Many authorities [1] regard **Rheumatoid arthritis** and **Osteo-arthritis** (arthritis deformans) as entirely different conditions. They maintain that, in the latter condition, the osteophytic outgrowths and the erosion of the central portions of the cartilages are specially characteristic, and that these may be entirely absent from cases of rheumatoid arthritis.

PROLIFERATIVE OSTEO-ARTHRITIS DEFORMANS (Spondylitis Deformans).—In this condition, which is not strictly a disease confined to the joints, bony outgrowths occur at the articular margins, especially those of the vertebræ, or at other parts of the bone. They may cause considerable deformity, and may lead to extensive ankylosis (*see* fig. 496). If occurring during the period of growth, deformities of the spine may arise, and serious effects may be produced by pressure on nerve-roots, etc. The disease is not confined to the human subject, but is found also in horses, cattle, and other animals.

NEUROPATHIC ARTHROPATHY.—This term is applied to certain destructive and proliferative changes which occur in joints in association with various nervous diseases, *e. g.* locomotor ataxia, syringomyelia, etc.; and

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[1] A. E. Garrod, " Rheumatoid Arthritis, Osteo-arthritis, Arthritis Deformans," *A System of Medicine,* Albutt and Rolleston, Vol. III., p. 3, Macmillan & Co., Ltd.. 1907.

which are supposed to be due to neurotrophic disturbances. The special joints affected seem to have some relationship to the particular region of the spinal cord in which the degenerative lesions in the nerve-cells and tracts or fibres occur. Thus, in locomotor ataxia, the joints of the lower extremities, and especially the knee-joints, are affected in a large proportion of the cases; whereas in syringomyelia, which is found usually in the cervical region of the cord, the joints of the upper extremities are generally involved. The pathological changes in the joints, in these cases, are essentially similar to those seen in the various forms of chronic arthritis—viz. destruction of the cartilages, and proliferative overgrowth of the synovial membrane and of the articular ends of the bones, and, in some cases, marked atrophic changes. Rapid effusion may take place into the cavity of the knee-joints (Charcot's joints) when they are thus involved in the course of locomotor ataxia.

CHRONIC HYPERTROPHIC (PULMONARY) OSTEO-ARTHRO-PATHY.—This condition, the pathology of which is at present unknown, is characterised by an enlargement of the distal extremities of the terminal phalanges of the fingers and toes, and also by swelling of the bones of the wrists and ankles, elbows, knees, and even of the distal ends of the radius, ulna, tibia, fibula, etc. The condition is associated with chronic diseases of the lungs and pleura; and an analogous condition may be found in congenital diseases of the heart, especially pulmonary stenosis and incomplete development of the inter-ventricular septum.

TUBERCULOUS DISEASE OF JOINTS.—This disease, which is of most frequent occurrence in children, commences

Fig. 496.—*Osteo-arthritis Deformans (Spondylitis Deformans) of the Vertebræ*, producing ankylosis. Note the nodular masses of new bone, bridging across the intervertebral discs, and costo-vertebral joints. (Edinburgh University Anatomical Museum. Catalogue N., Os. F. c. 2.)

generally in the synovial membrane; though, in some cases, the bone is invaded first, and the joint becomes involved by direct extension through the synovial membrane or articular cartilage. In either form,

the synovial membrane becomes thickened and gelatinous in appearance (the so-called **gelatinous degeneration**), and shows numerous outgrowths, especially of the synovial fringes. At a later stage, the membrane is converted into a soft, pultaceous material, which covers the articular surface. The articular cartilages become invaded, softened, eroded, or ulcerated, especially towards the central part. Even when the destructive change has become very pronounced, pinkish, semi-caseous granulations may be seen at the margins. The bone becomes invaded, and the medullary spaces are filled with tuberculous granulation-tissue, and widened by absorption of the bony trabeculæ. Thus, the bone becomes softened and very spongy, and extensive areas of destruction by **caries** may occur. The ligaments and tissues round the affected joint become œdematous, swollen, and converted into tuberculous granulation-tissue. Spontaneous rupture of the ligaments may occur; and sinuses, communicating with the surface and leading into the cavity of the joint, are a frequent manifestation of the condition. **On microscopical examination of the tissues,** typical tubercle-follicles, in all stages of development, may be found.

In the neighbourhood of the tuberculous joint, there is, in many cases, in addition to the destructive changes, a considerable amount of irritative new formation of bone, and, thus, irregular outgrowths may be produced.

SYPHILIS OF JOINTS.—In **acquired syphilis,** the joints are sometimes affected, and a **chronic arthritis,** characterised by the presence of gummata in the synovial membranes or in the tissues round the joint, is seen. Cicatricial contraction may occur, producing irregular scars. A syphilitic **chondro-arthritis,** in which the synovial membrane is thickened and its fringes are hypertrophied, has been described. The cartilages may shew pitted erosions; and erosion and eburnation of bone may be present. The synovial membranes frequently shew gummatous infiltration.

In **congenital syphilis,** there may be arthritis with exudation into the joint-cavity, which may come on very rapidly, and which is very often bilaterally symmetrical. The capsule of the joint may become thickened, and ulceration of the cartilages may occur. Gummatous infiltration of the tissues round the joint may extend into the cavity, and give rise to inflammatory changes there. "Charcot" and other forms of affection of the joints, seen in locomotor ataxia, which most authorities regard as due to syphilis, are referred to on pp. 1008 and 1054–5.

LOOSE BODIES IN THE JOINTS.—These may occur in otherwise apparently **healthy joints,** in which case they are usually the result of traumatism—portions of cartilage, or cartilage and bone, becoming detached and lying free in the joint-cavity, or remaining partially adherent at their site of origin. These bodies may, in the knee-joint, become arrested between the anterior surface of the bones

and the capsular ligament, and produce sudden "locking" of the joint. They may also give rise to recurrent attacks of synovitis.

In diseased joints, loose bodies may also occur, and may be composed of detached fragments of cartilage, hypertrophied synovial fringes, bone, or, perhaps most commonly, either wholly or in part, of fibrinous exudate. The first three varieties are seen especially in cases of arthritis deformans; whilst the last-mentioned are of common occurrence in arthritis with exudation (e. g. tuberculous arthritis), and constitute the so-called **rice** or **melon seed-bodies.**

Strangeways [1] points out, in an interesting paper, that the staining-properties and the appearance of the cells of these bodies on section shew that they are alive at the time of their removal from the joint-cavity. He maintains that they are nourished by the synovial fluid.

HÆMOPHILIC JOINT-DISEASE.—Effusion of blood may take place into the knee, or, less commonly, into other joints, in cases of hæmophilia. The blood may be completely absorbed, but, in some cases, adhesions are left; and, in others, changes like those seen in osteoarthritis may develop.

[1] Strangeways: "The Nutrition of Articular Cartilage," *Brit. Med. Jour.,* May 15, 1920, p. 61.

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DISEASES OF THE VOLUNTARY MUSCLES

RUPTURE of muscles—apart from injury—may arise from sudden or violent contraction, and may involve only a few fibres or numerous strands of the muscle. The condition is usually accompanied by a considerable amount of hæmorrhage and swelling.

HÆMORRHAGES into and between the muscle-fibres are common in fevers, e. g. in cerebro-spinal fever, in hæmorrhagic diseases, such as scurvy, purpura, and hæmophilia, in septicæmia, and in cases where there is an excessive action of the muscles, e. g. in tetanus and other convulsive disorders. Usually, the hæmorrhagic areas are minute; but, in scurvy and in hæmophilia, large extravasations may be found, which tear and push aside the muscle-fibres. Extensive hæmorrhage also takes place in rupture of muscle.

ŒDEMA.—The inter-muscular connective tissue, and the muscles themselves, may shew considerable œdema in Bright's disease, in anæmia, and in other conditions in which œdema is generally found in the other tissues.

DEGENERATIONS :—

(1) **CLOUDY SWELLING** is common in general infective diseases, such as fevers, etc. The muscle-fibres become swollen, pale and opaque, as if they had been immersed in hot water. Microscopically, the striation becomes obscured or even lost, and the sarcoplasm appears more granular than normal.

(2) **FATTY DEGENERATION** follows disuse from paralysis and other causes; it may be a sequel of cloudy swelling; or it may be a primary condition arising as a result of toxic poisoning in acute fevers, e. g. diphtheria, and in general septic diseases. It occurs to a marked degree in phosphorus-poisoning. To the naked eye, the muscle has a yellowish colour, and tears very readily. On microscopical examination, oil-droplets are seen in the muscle-fibres. In certain disorders associated with an abnormal carbohydrate metabolism, especially **diabetes mellitus,** there may be a great increase in the amount of interstitial fat present in the muscle, without much evidence of true fatty degeneration.

(3) **WAXY or AMYLOID DEGENERATION** is said to occur in the connective tissue of the muscle-bundles.

(4) **CALCIFICATION** is sometimes found as a sequel of other degenerative changes in the muscle itself; but it more commonly originates in the inter-muscular tissue, secondary to non-suppurative or suppurative inflammatory conditions. It may also occur in, and around, parasitic cysts, e. g. those of *Trichinella spiralis.*

(5) **PIGMENTATION.**—An increase in pigment is very common in muscle which is undergoing atrophy—the pigment appearing in the form of yellowish granules, and accumulating especially around the poles of the nucleus.

NECROSIS of muscle-fibres occurs in fevers and other toxic diseases, and also may result from their invasion or compression by malignant 'growths. The muscle-fibres appear more homogeneous and are somewhat swollen, their nuclei having lost the power of taking up basic stains.

FIG. 497.—Necrosis (so-called Zenker's Degeneration) of Muscle (rectus abdominis) in typhoid fever. × 200.

, **COAGULATION-NECROSIS**—(Zenker's Degeneration)—a condition which is, by some authors, incorrectly called " hyaline degeneration "— occurs especially in typhoid fever and similar diseases. The muscle-fibres are swollen, present a homogeneous appearance, have lost their striation, and finally break up into small translucent masses which gradually become absorbed. Hæmorrhages into the degenerated areas are not uncommon. The abdominal muscles, the psoas, and the adductors of the thigh, are the usual sites of this change. Though occurring especi-, ally in typhoid fever, a similar coagulation-necrosis may occur in all

severe fevers, such as smallpox, scarlet fever, etc., as well as in a variety of other conditions.

ATROPHY :—

(1) **Simple Atrophy** of muscle occurs in old age : in all wasting diseases, such as tuberculosis, cancer, diabetes mellitus, etc. : in cases of starvation : and in most acute infective diseases, *e. g.* fevers. It arises also as a result of diseases of joints, as in the muscles of a limb where the joint is ankylosed : or as a secondary result following over-use. The latter form is well illustrated by the atrophy of the sterno-mastoids, the scaleni, and the other extraordinary muscles of respiration, which supervenes upon the hypertrophy of these muscles, in long-standing cases of respiratory embarrassment : and from the prolonged over-use of certain muscles in some trade-occupations and sports.

Microscopical examination of these wasted muscles shews a considerable increase in the number of the nuclei, which are often arranged in groups at the periphery of the fibre. The transverse striation is frequently poorly marked and, in some instances, absent. Some of the fibres have a hyaline appearance, while others become granular. There is often a relative increase in the amount of interstitial fibrous tissue ; but the amount of fatty tissue varies very much in different cases—in some it is entirely absent, in others it is increased in amount.

(2) **Neuropathic Atrophy.**—Under this term are included all the forms of muscular atrophy which result **from disease of the peripheral or central nervous system.** The wasting may be of the muscle as a whole, or only certain individual fibres may be involved. Special muscle-groups are affected in different cases, according to the site of the lesion in the nervous system ; and the extent and degree of wasting are also partly dependent on the same factor. Thus, **in disease or injury of the peripheral nerves,** the wasting is confined to the muscles supplied by the nerve ; and the degree of atrophy may vary considerably, according to the extent and nature of the lesion. Thus, in neuritis, the atrophy may be slight, or it may be very marked ; whilst, in cases of injury, where the nerve has been cut or torn across, the atrophy may be rapidly produced and extreme in degree. **In disease of the spinal motor cells and their axis-cylinder processes in the cord,** there may be extreme wasting of the muscles ; or the atrophy may be partial and only involve a few individual fibres—this variation depending, to a certain degree, on the extent of the destruction in the spinal cord, and the number of the motor cells involved. Atrophy as the result of changes **in the lower neurons,** is seen in infantile paralysis, progressive muscular atrophy, and amyotrophic lateral sclerosis. **In disease of the upper neurons,** the wasting is usually less rapid and less extreme, as the neurotrophic influence of the lower neurons is still present. Usually, however, owing to the loss of the influence of the cells of the

upper neurons, and consequent loss of voluntary movement, the muscles—being deprived of their function—also undergo atrophy. The affected muscle-fibres are generally pale and flabby, and, **on microscopical examination,** the striation may be obscured, and the fibres fragmented; and coagulation-necrosis, or fatty degeneration, may be present. Not uncommonly, there is a proliferation of the connective tissue between the atrophied muscle-fibres; and an excessive accumulation of fat may also
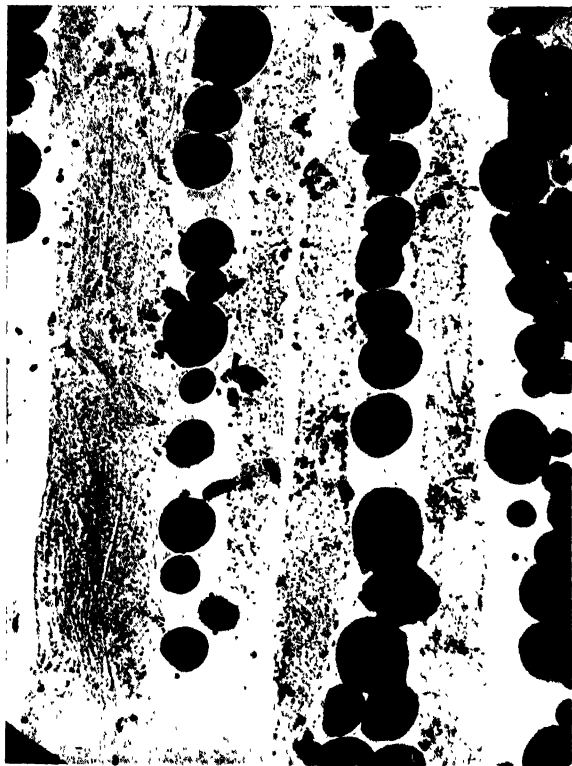
FIG. 498.—*Pseudo-hypertrophic Muscular Atrophy.* Longitudinal section of erector spinæ muscle. (See text.) × 200.

take place in the same situation. This adipose condition is often very marked.

(3) **Myopathic Muscular Atrophies (the Muscular Dystrophies),** the pathology of which is unknown, are generally described as occurring in two main forms—the **atrophic** and the **pseudo-hypertrophic** (*see* pp. 1003–4); but Erb has shewn that there is no sharp division between these forms.

He subdivides the disease into two groups :—

i. Those cases which occur in infancy.

ii. Those which occur in youth and adult life.

He maintains that, in all cases, there is, first, hypertrophy of the muscle-fibres, and a slight increase in the amount of connective tissue. Later, atrophy supervenes—the muscle-fibres become vacuolated and fragmented, the sarcolemma-nuclei greatly increased in numbers, and the connective tissue in and between the bundles increased in amount. Fat is deposited in this new connective tissue in varying degree—being sometimes so abundant as to produce very large masses of fatty tissue, which give to the affected part the appearance of hypertrophy.

. In different instances special groups of muscles are affected. Thus, in some of the cases occurring in infancy, the muscles of the face shew the involvement early in the disease; whilst in others, the facial muscles seem to escape.

The changes are best seen in the so-called **pseudo-hypertrophic** forms, and, in these cases, particularly in the muscles of the calves. The extensors of the leg, the glutei, the lumbar muscles, the deltoid, and the triceps, are the next most frequently involved. Except in the special instances already mentioned, the muscles of the neck, face, and forearm rarely suffer.

INFLAMMATION :—

Various forms of inflammation of muscle have been described, but it is sufficient to distinguish between the non-suppurative and the suppurative types.

(*a*) **Non-Suppurative Myositis** is usually the result of traumatism : or secondary to inflammation of neighbouring structures, *e. g.* the skin, bones, joints, mucous membranes, etc. It is frequently primary, due to some infective agent, *e. g.* that seen in rheumatism; and it is also associated with trichinelliasis (trichinosis). It presents the ordinary phenomena of inflammation in other situations, the muscles becoming swollen, congested, and œdematous, and infiltrated with polymorphonuclear leucocytes (Plate XVII, fig. 1).

In cases in which the inflammatory reaction is due to the irritation of a foreign body, such as a bullet, a piece of clothing, catgut-ligatures, etc., and in which sepsis is not pronounced, the muscle-fibres tend to lose their striation, to become homogeneous in appearance, and eventually to disappear. The sarcolemma-nuclei undergo proliferation, and a characteristic feature is the production of large mononucleated (Plate XVII, fig. 2) and also irregular multinucleated cells—cells concerned apparently in the process of absorption.

(*b*) **Suppurative or Purulent Myositis** may follow suppurative affections in the neighbouring structures; or may be hæmatogenous in origin—the organisms being carried by the blood-stream and deposited in the muscles, for example, in cases of pyæmia, erysipelas, purulent arthritis, etc. The pus may burrow in various directions between, and in, the muscle-bundles; and the muscle-fibres become swollen, softened, and necrosed. In the

DESCRIPTION OF PLATE XVII

PLATE XVII

FIG. 1.—Muscle-fibres adjoining a wound (3 days). × 700. (*a*) Healthy muscle; (*b*) degenerated muscle which is being penetrated and absorbed by both polymorpho-nuclear leucocytes and mononucleated cells. (From thesis by J. W. Dawson, M.D.)

FIG. 2.—Muscle almost replaced by phagocytic mononucleated cells. Note the remains of muscle-fibres in the phagocytes. (From thesis by J. W. Dawson M.D.)

Plate XVII. Vol. II.
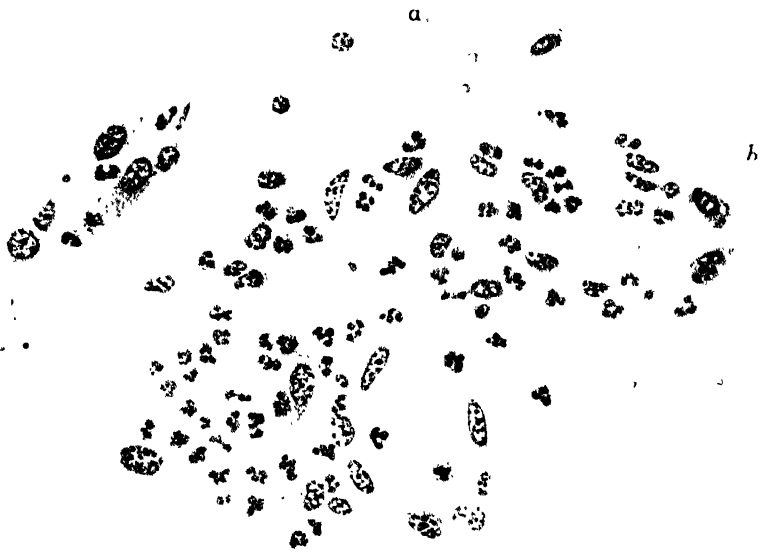
Fig 1.
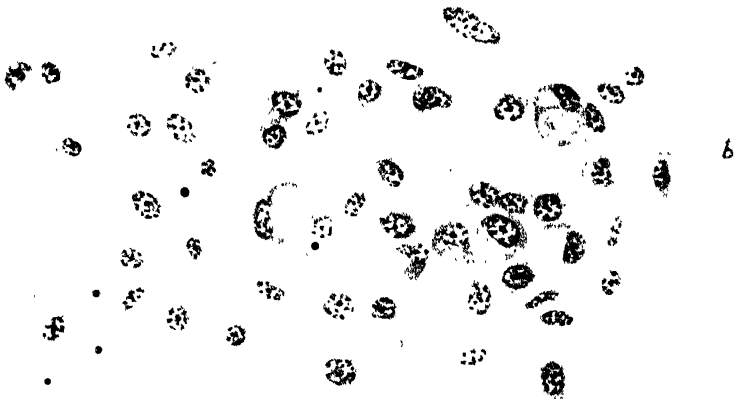
Fig 2.

more intense cases, hæmorrhage and gangrene may occur; and the muscle may be completely destroyed.

MYOSITIS OSSIFICANS.—In this disease, the formation of bone occurs in the muscles. The condition may follow an injury, or such degenerative and necrotic changes as result from acute inflammation. In the process of repair of these damaged parts, granulation-tissue is developed; and this may undergo myxomatous change, or calcification; or it may become the seat of actual formation of bone. The muscles most frequently affected are the deltoid and pectoral muscles, the adductors of the thighs, and the other muscles of the arms and legs. The bone may be in the form of irregular nodules, needle-like masses, or plates.

A progressive form **(Myositis Ossificans Progressiva)** occurs especially in young subjects, and affects the muscles of the neck, back, and thorax, spreading gradually over the entire body. The cause of this form is unknown.

TUBERCULOSIS, as a primary condition in muscle, is rare; but secondary infiltration from neighbouring structures such as tuberculous bones, joints, skin, serous membranes, etc., is common—producing abscesses and other destructive changes in the muscles. The psoas and lumbar abscesses which result from tuberculous disease of the vertebræ, and abscesses in the neighbourhood of the hip-joint, are common examples of this secondary infiltration.

SYPHILIS.--Some of the more chronic forms of myositis may be syphilitic in origin, but the most frequent manifestation of syphilis in the muscles is the presence of gummata. These may form large tumour-like masses, presenting a central area of caseation, and a peripheral zone of vascular granulation-tissue. Between these two zones, there are usually several layers of fibrous tissue, more or less dense in character. The vessels may shew marked peri- and end-arteritis. The muscles most commonly affected are the biceps, the muscles of the neck and back, the tongue, and the sphincter ani.

ACTINOMYCOSIS, MYCETOMA, GLANDERS, and LEPROSY, may involve the muscles in the vicinity of the original lesion.

TUMOURS of muscle are usually secondary; though primary **sarcomata** are described. The **fibromata, lipomata, myxomata, osteomata,** etc., found in muscle, take their origin usually from the interstitial fibrous tissue, and not from the muscle-fibres. **Rhabdo-myomata**—often teratomatous in origin—and mixed **teratomatous** tumours containing striped muscle are also found. **Sarcomata** and **carcinomata** occur as **secondary growths,** and commonly are the result of direct spread from tumours in the vicinity.

PARASITES.—*Trichinella spiralis, Cysticerus cellulosœ,* and **Hydatids** have been found. *These are fully described in Chapter XI.*

For **Rigor Mortis** *see* p. 87, and **Healing and Regeneration of Muscle;** p. 223, *General Pathology,* and Plate XVII, figs. 1 and 2, p. 1064.

DISEASES OF THE TENDONS, TENDON-SHEATHS, AND BURSÆ

Only a brief reference to these is required here, as the subject is fully dealt with in works on Surgery.

RUPTURE OF TENDONS.—Tendons may be torn from their attachments, or rupture of them (e. g. of the tendon of the plantaris muscle, the tendo Achillis, etc.) may take place especially if they are the seat of previous disease.

DISPLACEMENTS of tendons, e. g. of the biceps, or of one of the peronei muscles, occasionally occur.

HÆMORRHAGE INTO TENDON-SHEATHS sometimes results from injury, from severe inflammation, or from other causes.

CALCIFICATION follows other degenerative or chronic inflammatory lesions. **GOUTY DEPOSITS** of urates are found in and around tendons and their sheaths.

INFLAMMATION OF TENDON-SHEATHS or **TENO-SYNOVITIS,** is of greater importance, and the pathological changes produced are analogous to those caused by inflammation in other closed serous sacs. Teno-Synovitis may be **acute** or **chronic—dry, with effusion of fluid, or suppurative.**

(*a*) **Acute Non-suppurative Teno-Synovitis** may be **traumatic,** c. g. from over-action, or from sprains; or **infective** in origin, e. g. from infection with the organisms of acute rheumatism, gonorrhœa, etc. Gonorrhœal cases are generally suppurative; but pus is never developed in uncomplicated rheumatic cases. Acute inflammation may also occur in gout. In such cases, the amount of fluid exudate varies greatly.

(*b*) **Suppurative Teno-Synovitis** due to the involvement of the tendon-sheaths in infected wounds; to the extension into them of local suppurative conditions, e. g. in whitlow; or as a part of a more generalised infection, e. g. in gonorrhœal and other septicæmias, and in pyæmia and analogous conditions is frequently found.

(*c*) **Chronic Teno-Synovitis** may be a sequel of acute inflammation; but, more commonly, it is **tuberculous** or **syphilitic** in origin. The pathological changes in **tuberculous teno-synovitis** are practically identical with those found in tuberculous arthritis. The chief varieties are (1) a gelatinous form, in which the tendon and its sheath become softened and jelly-like: (2) a variety accompanied by serous effusion: and (3) a form which leads to the production of " chronic abscess." In **Syphilis,** the tendons and their sheaths are sometimes the seat of a comparatively acute inflammatory attack, but, more frequently, the process is a chronic one. Gummatous formation occurs in the substance of tendons, and interstitial overgrowth is also a sequel of syphilis.

These various forms of teno-synovitis may be accompanied, or followed by, the production of **adhesions.** The intenser forms of inflammation, especially if suppurative, may lead to **necrosis** of the affected tendon. **Cicatricial contraction,** . producing deformities, also follows in certain instances.

TUMOURS OF TENDON.—Primary tumours are rare. Myxomas, fibromas, chondromas, osteomas, and sarcomas, have been described. **Secondary infiltration** by malignant tumours of neighbouring structures may, of course, take place.

DISEASES OF BURSÆ :—

Inflammatory conditions of these are of importance, and are fully discussed in surgical textbooks.

Acute Bursitis may be non-suppurative, suppurative, or hæmorrhagic. In the first-mentioned of these, effusion is usually, though not always, a characteristic feature. **Chronic Bursitis** may be secondary to previous acute disease, or it may be tuberculous or syphilitic. Both acute and chronic forms are found in gouty subjects.

Tumours, such as fibromas, myxomas, chondromas, and sarcomas, occasionally arise from bursæ.

" **Adventitious Bursæ** " are developed over bony prominences subject to pressure and irritation, e. g. in cases of bunion, or on the shoulders, necks, or heads of porters who are accustomed to carry heavy weights on these parts. Such false bursæ are very liable to inflammation.

" **Ganglion.**"—In this condition, cavities, sometimes of considerable size, and containing clear, white-of-egg-like fluid, or, perhaps more characteristically, a transparent, colourless, material resembling glycerine jelly, are developed in the neighbourhood of joints and tendon-sheaths—most commonly about the dorsal aspect of the wrist. Their origin is much discussed. They have usually been regarded as narrow-necked diverticula growing from the synovial membranes of joints or of tendon-sheaths; but, more recently, the view has been advanced that they are myxomatous in nature, and arise from the connective-tissue elements in the neighbourhood of, but not constituting part of, the joints or tendon-sheath.

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